3605227-4-00-01

MEDWATCH

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

OLUNTARY reporting
lth professionals of adverse
events and product problems

CDER

Page 1 of 1

CDER

Form Approved: OMB No. 0910-0291 Expires:12/31/5
See OMB statement on revers

FDA Use Only H Pad

Triage unit sequence # 131890

Patient information

Patient identifier	2. Age at time of event: / or Date of birth:	3. Sex	4. Weight
383727 In confidence	81 / [redacted]	☐ female ☑ male	___ lbs or 76 kgs

B. Adverse event or product problem

1. ☑ Adverse event and/or ☐ Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)
- ☐ death ___ (mo/day/yr)
- ☐ life-threatening
- ☑ hospitalization – initial or prolonged
- ☐ disability
- ☐ congenital anomaly
- ☐ required intervention to prevent permanent impairment/damage
- ☐ other: ___

3. Date of event (mo/day/yr): 9/11/00

4. Date of this report (mo/day/yr): 10/25/00

5. Describe event or problem

Prescribed Celebrex for rotator-cuff repair on 8/31/00.

Admitted 9/11/00 with N&V(+) stool coffee ground emesis and endoscopically proven multiple small gastric ulcers and intraluminal blood.

6. Relevant tests/laboratory data, including dates

Hb (8/24) 13.7 → 9.0 (9/11)
Hct " 41.1 → 30 "

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

Diabetes
osteoarthritis
BPH
(no history GI bleed)
other meds: Saw Palmetto

CT 131890

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
- #1 Celebrex (dose?) QD.
- #2 It also admits taking Advil simultaneously

2. Dose, frequency & route used
- #1 (dose?) QD
- #2 Advil (dose?)

3. Therapy dates (if unknown, give duration) from/to (or best estimate)
- #1 8/31/00 – 9/11/00
- #2 ?

4. Diagnosis for use (indication)
- #1 Rotator cuff repair
- #2 osteoarthritis

5. Event abated after use stopped or dose reduced
- #1 ☑ yes ☐ no ☐ doesn't apply
- #2 ☑ yes ☐ no ☐ doesn't apply

6. Lot # (if known)
- #1
- #2

7. Exp. date (if known)
- #1
- #2

8. Event reappeared after reintroduction
- #1 ☐ yes ☐ no ☑ doesn't apply
- #2 ☐ yes ☐ no ☑ doesn't apply

9. NDC # (for product problems only)
- –
- –

10. Concomitant medical products and therapy dates (exclude treatment of event)

D. Suspect medical device

1. Brand name

2. Type of device

3. Manufacturer name & address

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MEDWATCH CTU

4. Operator of device
- ☐ health professional
- ☐ lay user/patient
- ☐ other: ___

5. Expiration date (mo/day/yr)

6.
- model # ___
- catalog # ___
- serial # ___
- lot # ___
- other # ___

7. If implanted, give date (mo/day/yr)

8. If explanted, give date (mo/day/yr)

9. Device available for evaluation? (Do not send to FDA)
☐ yes ☐ no ☐ returned to manufacturer on ___

10. Concomitant medical products and therapy dates (exclude treatment of event)

NOV 0 1 2000

E. Reporter (see confidentiality section on back)

1. Name, address & phone #
[redacted], PharmD
[redacted] Rd.

2. Health professional? ☑ yes ☐ no

3. Occupation: Pharmacist

4. Also reported to
- ☐ manufacturer
- ☐ user facility
- ☐ distributor

5. If you do NOT want your identity disclosed to the manufacturer, place an " X " in this box. ☐

FDA

Mail to: MEDWATCH
5600 Fishers Lane
Rockville, MD 20852-9787

or FAX to:
1-800-FDA-0178

FDA Form 3500 (6/93)

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

Individual Safety Report

3629000-6-00-01

134103

MEDWATCH

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

For VOLUNTARY reporting by health professionals of adverse events and product problems

CDER

CDER

[redacted] Form approved; OMB No. 0910-0291 Expires: See OMB statement on reverse.

FDA Use Only

Triage unit

sequence #

A. Patient information

1. Patient identifier	2. Age at time of event: or Date of birth:	3. Sex	4. Weight
XX In confidence	42y	☐ female ☑ male	____ lbs or ____ kgs

B. Adverse event or product problem

1. ☑ Adverse event and/or ☐ Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)
- ☐ death ____ (mm/dd/yyyy)
- ☐ life-threatening
- ☑ hospitalization – initial or prolonged
- ☐ disability
- ☐ congenital anomaly
- ☐ required intervention to prevent permanent impairment/damage
- ☐ other: ____

3. Date of event (mm/dd/yyyy): 9-13-00

4. Date of this report (mm/dd/yyyy): 12-13-00

5. Describe event or problem (up to a total of 8400 characters allowed)

GASTROINTESTINAL BLEEDING: HEMATOCHEZIA. Patient w/ familial polyposis S/P colon resection presents to hospital w/ 2 week h/o LUQ pain & bright red blood on tissue following 3 weeks of increased ibuprofen 200mg use (about 10 QD) for increased body/stomach pain. Bleeding stopped after stopped taking Ibuprofen. EXAM: rectal guiaic negative. GI bleed felt probably from antral erosions (2 small ID'd from EGD) d/t increased NSAID use. Discharged on Lansoprazole & Rofecoxib.

DISCHARGED 2 DAYS P ADMISSION.

6. Relevant tests/laboratory data, including dates (a total of 1000 characters allowed)

7. Other relevant history, including preexisting medical conditions (up to a total of 500 characters allowed)

DSS

DEC 14 2000

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CTV134103

C. Suspect medication(s)

1. Name (Product Name)	(Labeled Strength)	(Mfr/Labeler)
#1 IBUPROFEN	/	/
#2	/	/

2. Dose/Frequency/Route used	3. Therapy dates (if unknown, give duration) From	To (or best estimate)
#1 / /	#1	
#2 / /	#2	

4. Diagnosis for use (separate indications with commas)
#1
#2

5. Event abated after use stopped or dose reduced
#1 ☐ yes ☐ no ☐ Coe ad
#2 ☐ yes ☐ no ☐ do ap

6. Lot # (if known)
#1
#2

7. Exp. date (if known)
#1
#2

8. Event reappeared after reintroduction
#1 ☐ yes ☐ no ☐ co ad
#2 ☐ yes ☐ no ☐ co ap

9. NDC # (for product problems only)
- –

10. Concomitant medical products and therapy dates (up to a total of 1000 charac

D. Suspect medical device

1. Brand name

2. Type of device

3. Manufacturer name & address

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4. Operator of device
- ☐ health professional
- ☐ lay user/patient
- ☐ other: ____

5. Expiration date (mm/dd/yyyy)

6.
- modal # ____
- catalog # ____
- serial # ____
- lot # ____
- other # ____

7. If implanted, give d (mm/dd/yyyy)

8. If explanted, give d (mm/dd/yyyy)

9. Device available for evaluation? (Do not send device to FDA)
☐ yes ☐ no ☐ returned to manufacturer on ____ (mm/dd/yyyy)

10. Concomitant medical products and therapy dates (up to a total of 1000 charac

E. Reporter (see confidentiality section on back)

1. Name [redacted] phone # [redacted]

Address [redacted] Med Center [redacted] St., [redacted]

E-mail (for electronic acknowledge

2. Health professional? ☑ yes ☐ no

3. Occupation: Pharmacist

4. Also reported to
- ☐ manufacturer
- ☐ user facility
- ☐ distributor

5. If you do not want your identity disclosed to the manufacturer, place an "X" in this box. ☑

FDA

Mail to: MEDWATCH, 5600 Fishers Lane, Rockville, MD 20852-9787

or FAX to: 1-800-FDA-0178

MEDWATCH
THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

Individual Safety Report

3641929-1-00-01

MEDWatch

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

Approved by FDA on 10/20/93

Triage unit sequence # 135021

CDER

A. Patient Information

1. Patient Indentifier [redacted] | 2. DOB: [redacted] AGE: 87 yrs | 3. Sex: MALE | 4. Weight: 35.4 kg

B. Adverse Event or Product Problem

1. [X] Adverse Event [ ] Product problem

2. Outcomes attributed to adverse event
- [ ] death:
- [X] life-threatening
- [X] Hospitalization initial or prolonged
- [ ] disability
- [ ] congenital anomaly
- [X] required intervention to prevent impairment/damage
- [ ] other

3. Date of event: 07/23/00

4. Date of this report: 11/10/00

5. Describe event or problem
gastrointestinal bleeding

6. Relevant test/laboratory data, including dates
PLEASE SEE ATTACHED

7. Other relevant History, including preexisting medical conditions
87 year old male with a history of peptic ulcer disease in 1997, dementia, and supraventricular tachycardia. The patient was admitted after an episode of near syncope followed by melena that resulted in hospital admission in
PLEASE SEE ATTACHED

Mail to: MedWatch
5600 Fishers Lane
Rockville, MD 20852-9787

or FAX to:
1-800-FDA-0178

FDA Form 3500

C. Suspect Medication(s)

1. Name
#1 : IBUPROFEN

2. Dose, frequency & route used
#1:

3. Therapy dates
#1 :

4. Diagnosis for use (indication)
#1:

5. Event abated after use stopped or dose reduced?
#1: [N/A]

6. Lot # (if known)
#1:

7. Exp. date
#1:

8. Event reappeared after reintroduction
#1: [ ]

9. (Not applicable to adverse drug event reports)

10. Concomitant medical products/therapy dates (exclude treatment)
VERAPAMIL SR 180 MG TAB
BACTRIM DS EQUIVALENT TAB
ACETAMINOPHEN 500 MG CAPLET
PLEASE SEE ATTACHED

D. Suspect Medical Devices

Note: Please use the actual MedWatch form if the event involves a suspected device as well as a suspect drug

E. Reporter

1. Name, address & phone #: PHARMACY SERVICE
1201 N W 16TH STREET
MIAMI, FLORIDA 33125 324-4455

2. Health professional? [YES]

3. Occupation: PHARMACY RESID

4. Reported to Mfr. [NO]

5. If you don't want your identity disclosed to the Manufacturer, place an "X" in the box. [X]

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

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MEDWATCH CTU

JAN 0 5

CTV135021

Section B. Part 6. Relevant Test/Laboratory Data Continued:
TEST: HGB RESULTS: L 9.1 g/dL H:17.2/L:12.8 COLLECTION DATE: 7/25/00@01:19
TEST: HCT RESULTS: L 27.4 % H:48.2/L:40.2 COLLECTION DATE: 7/25/00@01:19
TEST: HGB RESULTS: L 9.4 g/dL H:17.2/L:12.8 COLLECTION DATE: 7/24/00@07:00
TEST: HCT RESULTS: L 28.3 % H:48.2/L:40.2 COLLECTION DATE: 7/24/00@07:00
TEST: HGB RESULTS: L 10.8 g/dL H:17.2/L:12.8 COLLECTION DATE: 7/23/00@07:00
TEST: HCT RESULTS: L 32.5 % H:48.2/L:40.2 COLLECTION DATE: 7/23/00@07:00

Section B. Part 7. Other Relevant History Continued
[redacted]. THe patient had been self-administering ibuprofen. The patient received two units of packed red blood cells and underwent upper endoscopy which showed a prepyloric ulcer with brown eschar, but no active bleeding at the time of the endoscopy. The patient remained hemodynamically stable after the transfusion and a transfer was coordinated by the family this facility.The patient underwent a second endoscopy which showed a 2 cm clean based ulcer in the duodenal bulb with duodenitis. The stomach had no ulcers. H-pylori was negative with CLO test. Throughout admission, the patient's hematocrit remained stable and the ulcer was treated with ranitidine and lansoprazole. He was discharged to a nursing home.

Section C. Part 10. Concomitant Drugs Continued
TIMOLOL 0.5% OPHTH SOL 15 ML
PILOCARPINE HCL 2% OPHTH SOL 15 ML
DORZOLAMIDE 2% HCL OPHTH SOL 5 ML

Individual Safety Report

3645657-8-00-01

DWATCH

ODUCTS REPORTING PROGRAM

BOX 8299
PHILADELPHIA, PA 19101

Approved by the FDA on 09/24/1999

Mfr report # HQ20643110CT2000

UF/Dist report #

FDA Use Only

A. Patient information

1. Patient identifier	2. Age at time of event:	3. Sex	4. Weight
[redacted] in confidence	or 69Yr Date of Birth:	[ ] female [X] male	UNK lbs or kgs

B. Adverse event or product problem

1. [X] Adverse event [ ] Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)

- [ ] death (mo/day/yr)
- [ ] life-threatening
- [X] hospitalization-initial or prolonged
- [ ] recovered
- [ ] disability
- [ ] congenital anomaly
- [ ] required intervention to prevent permanent impairment/damage
- [ ] other:

3. Date of event (mo/day/yr): 07/04/2000

4. Date of this report (mo/day/yr): 01/09/2001

5. Describe event or problem

Additional information received on 28-DEC-2000 from a physician upgraded the report to a 15 day. Initial information was received on 11-OCT-2000 from a 69 Yr old male. The patient's concurrent illnesses include Diabetes mellitus and Drug hypersensitivity (Penicillin allergy) with a past history of back surgery and right rotator cuff repair. Therapy with ADVIL (IBUPROFEN) (Tablet) for pain began weeks ago at 2 tablets daily. It is unknown if the patient was taking any concomitant medications. The patient was taken to the emergency room on 04-JULY-2000 after feeling ill and vomiting some blood (Haematemesis. Upon evaluation in the ER, the patient was found to have Heme positive stool with no abdominal tenderness. Blood tests revealed the following: Amylase normal at 46, BUN: 20 ,Creatinine: 0.7; total Bilirubin was elevated at 2.6 with only minimal elevations of the Alkaline phosphatase and SGOT; SGPT was normal; white blood cell count was 8.1, hemoglobin and hematocrit were 12.4 and 35 respectively;

(cont'd)

6. Relevant tests/laboratory data, including dates

See following page.

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

CONCURRENT CONDITIONS:
Diabetes mellitus NOS; Drug hypersensitivity

PAST CONDITIONS:
Operation NOS; Rotator cuff syndrome

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)

#1 ADVIL (IBUPROFEN, Tablet, 200 mg)

#2

2. Dose, frequency & route used	3. Therapy dates (if unknown, give duration)
#1 2 daily for weeks., Oral	#1 UNK
#2	#2

4. Diagnosis for use (indication)	5. Event abated after use stopped or dose reduced
#1 Pain NOS	#1 [ ] yes [ ] no [ ] doesn't apply UNK
#2	#2 [ ] yes [ ] no [ ] doesn't apply

6. Lot # (if known)	7. Exp date (if known)	8. Event reappeared after reintroduction
#1	#1	#1 [ ] yes [ ] no [X] doesn't apply
#2	#2	#2 [ ] yes [ ] no [ ] doesn't apply

9. NDC # - for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)

G. All manufacturers

1. Contact office - name/address

WHITEHALL-ROBINS
201 King of Prussia
Sixth Floor
Radnor, PA 19087-5114

Jill Robinson

2. Phone number: 6109644680

3. Report source (check all that apply)

- [ ] foreign
- [ ] study
- [ ] literature
- [ ] consumer
- [X] health professional
- [ ] user facility
- [ ] company representative
- [ ] distributor
- [ ] other:

4. Date received by manufacturer (mo/day/yr): 12/28/2000

5. (A)NDA 18-989
IND #
PLA #
pre-1938 [ ] yes
OTC product [X] yes

6. If IND, protocol #

7. Type of report

- [ ] 5-day
- [X] 15-day
- [ ] 10-day
- [ ] periodic
- [X] initial
- [ ] follow-up #

8. Adverse event term(s)

Oesophageal ulcer
Haematemesis

9. Mfr. report number: HQ20643110CT2000

E. Initial reporter

1. Name & address: [redacted] Dr [redacted] Road US

phone # [redacted]

2. Health professional? [X] yes [ ] no

3. Occupation: Physician

4. Initial reporter also sent report to FDA? [ ] yes [ ] no [X] unk

FDA Form 3500A (facsimile)

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

JAN 0 9 2001
DATE SENT TO FDA

JAN 1 0 2001

Individual Safety Report

3645657-8-00-02

EDWATCH

PRODUCTS REPORTING PROGRAM

Approved by the FDA on 09/24/1999

Mfr report #	HQ20643110CT2000
UF/Dist report #	
	FDA Use Only

BOX 8299
PHILADELPHIA, PA 19101

Box B.5 - Describe event or problem (Continuation)

platelets were normal at 165. The patient was treated with intravenous Zantac and lactated ringers.The patient was transfered to another hospital on 05-JULY-2000 where he underwent an esophagogastroduodenoscopy, which revealed an ulceration at the gastroesophageal junction (Oesophageal ulcer). The patient also had a"colonoscopy" done which revealed questionable non steroidal antiinflammatory drugs fundal gastritis and gastroesophageal junction ulcer and questionnable Advil pill ulcer. The patient was started on Prilosec and was discharged on 06-JULY-2000.

Box B.6 - Relevant test/laboratory data, including dates (Continuation)

Test Name / *Date*	*Result*	*Normal Range*
Alanine aminotransferase 07/00/2000	normal	-
Aspartate aminotransferase 07/00/2000	slightly elevated	-
Barium enema 07/00/2000	negative	-
Blood alkaline phosphatase NOS 07/00/2000	slightly elevated	-
Blood amylase 07/00/2000	46(normal).	-
Blood bilirubin 07/00/2000	2.6	-
Blood creatinine 07/00/2000	0.7	-
Blood in stool 07/00/2000	positive	-
Blood urea 07/00/2000	20	-
Colonoscopy 07/00/2000	Questionable nonsteroidal antiinflammatory drugs fundal gastritis.	-
Haematocrit 07/00/2000	35	-
Haemoglobin 07/00/2000	12.4	-
Oesophagoscopy 07/00/2000	ulceration at the gastroesophageal junction.	-
Platelet count 07/00/2000	165	-
White blood cell count 07/00/2000	8.1	-
X-ray with contrast upper gastrointestinal tract 07/00/2000	unknown	-

JAN 1 0 2001

Individual Safety Report

3655828-2-00-01

alth professionals of adverse
nts and product problems

Page ___ of ___ CDER Cber

FDA Use Only
Triage unit sequence # 136492

Patient information

1. Patient identifier: [redacted]9879 (confidence)
2. Age at time of event: / or / Date of birth: [redacted]
3. Sex: ☐ female ☐ male
4. Weight: ___ lbs or ___ kgs

B. Adverse event or product problem

1. X Adverse event and/or ☐ Product problem (e.g., defects/malfunctions)
2. Outcomes attributed to adverse event (check all that apply)
   - ___ death ___ (mo/day/yr)
   - ___ life-threatening
   - X hospitalization – initial or prolonged
   - ☐ disability
   - ☐ congenital anomaly
   - ☐ required intervention to prevent permanent impairment/damage
   - ☐ other:
3. Date of event: 11/28/00
4. Date of this report (mo/day/yr): 12/00
5. Describe event or problem

Admitted to MICU for hematemesis
Transfused 2 u PRBC,
Started sandostatin drip
PT had stopped taking Prevacid
DIC NSAIDS, Ticlid,
Restarted Prevacid 30mg BID

6. Relevant tests/laboratory data, including dates

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MEDWATCH CTU

7. Other relevant history, including preexisting medical conditions (e.g., allergies, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

CTU 136492

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
   - #1 Aspirin
   - #2 Ibuprofen (OTC)
2. Dose, frequency & route used
   - #1 325mg QOD
   - #2 Unknown Qhs
3. Therapy dates (if unknown, give duration) from/to (or best estimate)
   - #1
   - #2
4. Diagnosis for use (indication)
   - #1 pain
   - #2
5. Event abated after use stopped or dose reduced
   - #1 ☐ yes ☐ no ☐ doesn't apply
   - #2 ☐ yes ☐ no ☐ doesn't apply
6. Lot # (if known)
   - #1
   - #2
7. Exp. date (if known)
   - #1
   - #2
8. Event reappeared after reintroduction
   - #1 ☐ yes ☐ no ☐ doesn't apply
   - #2 ☐ yes ☐ no ☐ doesn't apply
9. NDC # (for product problems only) – –
10. Concomitant medical products and therapy dates (exclude treatment of event)

D. Suspect medical device

1. Brand name
2. Type of device
3. Manufacturer name & address
4. Operator of device
   - ☐ health professional
   - ☐ lay user/patient
   - ☐ other:
5. Expiration date (mo/day/yr)
6. model # / catalog # / serial # / lot # / other #
7. If implanted, give date (mo/day/yr)
8. If explanted, give date (mo/day/yr)
9. Device available for evaluation? (Do not send to FDA)
   ☐ yes ☐ no ☐ returned to manufacturer on ___ (mo/day/yr)
10. Concomitant medical products and therapy dates (exclude treatment of event)

E. Reporter (see confidentiality section on back)

1. Name, address & phone #
   [redacted] Blvd
   [redacted]
   DSS
   JAN 2 9 2001
2. Health professional? X yes ☐ no
3. Occupation: RPh
4. Also reported to
   - ☐ manufacturer
   - ☐ user facility
   - ☐ distributor
5. If you do NOT want your identity disclosed to the manufacturer, place an " X " in this box. ☐

Mail to: MEDWATCH, 5600 Fishers Lane, Rockville, MD 20852-9787 or FAX to: 1-800-FDA-0178

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

TH
W
BC
PHILADELPHIA, PA 19101

Individual Safety Report
3662506-2-00-01

WATCH
DUCTS REPORTING PROGRAM

Approved by the FDA on 09/24/1999

Mfr report # HQ6624531JAN2001
UF/Dist report #
FDA Use Only

A. Patient information

1. Patient identifier	2. Age at time of event:	3. Sex	4. Weight
[redacted] in confidence	or 34Yr Date of Birth: [redacted]	[X] female [ ] male	115 lbs or kgs

B. Adverse event or product problem

1. [X] Adverse event [ ] Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)

- [ ] death (mo/day/yr)
- [ ] life-threatening
- [ ] hospitalization-initial or prolonged
- [X] recovered
- [ ] disability
- [ ] congenital anomaly
- [ ] required intervention to prevent permanent impairment/damage
- [X] other: medically important

3. Date of event (mo/day/yr): 11/11/2000

4. Date of this report (mo/day/yr): 02/06/2001

5. Describe event or problem

Information was received on 26-JAN-2001 and 31-JAN-2001 from a 34 year old female consumer. The patient's concurrent illnessses include allergies to erythromycin and codeine, insomnia, migraine headaches, mitral valve prolapse, anemia. and bronchitis with a past history of tonsillectomy, rhinoplasty, and breast augmentation. Therapy with ADVIL MIGRAINE (IBUPROFEN) (Capsule, Liquid Filled) for migraine headaches began on 11-NOV-2000 and ceased on 11-NOV-2000. The dose regimen included one capsule by mouth twice daily at 5:00PM and 8:00PM respectively. Concomitant therapy included KLONOPIN (CLONAZEPAM), IRON (IRON), CEFTIN (CEFUROXIME AXETIL), and SINEQUAN (DOXEPIN HYDROCHLORIDE). At 11 PM on 11-NOV-2000 the consumer's mother noticed that the patient's speech was different (Dysarthria) and that she was experiencing symptoms of anaphylactic shock (Anaphylactic shock) such as confusion and going in and out of consciousness. The consumer reported that she was hoarse and unable to talk. Her mother noticed that

(cont'd)

6. Relevant tests/laboratory data, including dates

See following page.

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

CONCURRENT CONDITIONS:
Migraine NOS; Hypersensitivity NOS; Mitral valve prolapse; Insomnia NEC; Anaemia NOS; Bronchitis NOS

PAST CONDITIONS:
Tonsillectomy; Rhinoplasty; Breast enlargement

FEB 07 2001
DATE SENT TO FDA

FDA Form 3500A (facsimile)

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
#1 ADVIL MIGRAINE (IBUPROFEN, Capsule, Liquid
#2

2. Dose, frequency & route used
#1 1 Capsule 2x per 1 Day, Oral
#2

3. Therapy dates (if unknown, give duration)
#1 11/11/2000 to 11/11/200
#2

4. Diagnosis for use (indication)
#1 Migraine NOS
#2

5. Event abated after use stopped or dose reduced
#1 [X] yes [ ] no [ ] doesn't apply
#2 [ ] yes [ ] no [ ] doesn't apply

6. Lot # (if known)
#1 13001883
#2

7. Exp date (if known)
#1
#2

8. Event reappeared after reintroduction
#1 [ ] yes [ ] no [X] doesn't apply
#2 [ ] yes [ ] no [ ] doesn't apply

9. NDC # – for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)
See following Page.

G. All manufacturers

1. Contact office – name/address
WHITEHALL-ROBINS
201 King of Prussia
Sixth Floor
Radnor, PA 19087-5114
Jill Robinson

2. Phone number
610 9644680

CENTER FOR DRUG EVALUATION AND RESEARCH REC'D FEB 08 2001 CDR

Report source (check all that apply)
- [ ] foreign
- [ ] study
- [ ] literature
- [ ] consumer
- [ ] health professional
- [ ] user facility
- [ ] company representative
- [ ] distributor
- [ ] other

4. Date received by manufacturer (mo/day/yr): 01/26/2001

5. (A)NDA 20-402
IND #
PLA #
pre-1938 [ ] yes
OTC product [X] yes

6. If IND, protocol #

7. Type of report
- [ ] 5-day
- [X] 15-day
- [ ] 10-day
- [ ] periodic
- [X] initial
- [ ] follow-up #

8. Adverse event term(s)
Anaphylactic shock
Dysarthria
Sedation
Haematemesis

FEB 08 2001

9. Mfr. report number
HQ6624531JAN2001

E. Initial reporter

1. Name & address
[redacted], Ms.
[redacted], US
phone # [redacted]

DSS
FEB 09 2001

2. Health professional? [ ] yes [X] no

3. Occupation
UNK

4. Initial reporter also sent report to FDA [ ] yes [ ] no [X] unk

Box B.5 - Describe event or problem (Continuation)

she kept falling asleep with her eyes open (Sedation). At that point the patient felt that her throat was closing up. The patient has previously taken regular IBUPROFEN in the past without incident. On 12-NOV-2000, the patient went to the emergency room of [redacted] were she was treated and subsequently released. The patient continued to experience poor breathing [redacted], and on 12-NOV-2000 she went to [redacted] in [redacted] where she was treated with SOLUMEDROL and BENADRYL. The patient's labs during that emergency room visit were as follows: a blood pH of 7.404, a pCo2 of 35.1 mmHg, a pO2 of 104.6mmHg, a pAtm of 748, and HCO3 of 21.5 mmol/L, a blood base excess of -2.7 mmol/L, a ctHb of 12.4g/dL, an oxygen saturation of 98.5%, an O2Hb of 97.6%, a COHb of 0.7%, a MetHb of 0.1%, a HHb 1.5%, and a hct of 36% The patient's hoarseness abated, but she still felt that her throat was "closing up." During her stay at [redacted] the patient experienced damage to her right radial vein due to an improper intravenous line. The patient will subsequently have the vein removed. On 13-NOV-2000, the patient had vomited "old blood" (Haematemesis). The patient went to the hospital at [redacted] where she had a naso-gastric tube placed to drain the blood from her stomach. The patient recovered from her gastrointestinal bleed with the exception of a 10 pound weight loss. The patient's physician attributed her symptoms to therapy with ADVIL. On 26-NOV-2000, the patient was confirmed to have phlebitis at her old intravenous line site. Additional information has been requested.

Box B.6 - Relevant test/laboratory data, including dates (Continuation)

Test Name / *Date*	*Result*	*Normal Range*
Acid base balance		
11/12/2000	-2.7 mmol/L	-2.0 - 2.0
Blood bicarbonate		
11/12/2000	21.5 mmol/L	22 - 26
Blood carbon dioxide		
11/12/2000	35.1 mmHg	35 - 45
Blood pH NOS		
11/12/2000	7.404	-
Haematocrit		
11/12/2000	36 %	37 - 50
Haemoglobin		
11/12/2000	12.4 g/dL	13.5 - 18.5
Oxygen saturation		
11/12/2000	98.5 %	92.0 - 98.5
PO2		
11/12/2000	104.6 mmHg	80 - 100

Box C - Suspect medication(s) (Continuation from Lines #1 and #2 on original page)

1. Name (give labeled strength & mfr/labeler, if known)

1.1 Filled)

FEB 0 8 2001

Box C.10 - Concomitant medical products and therapy dates (exclude treatment of event) (Continuation)

Therapy Name	*Dose, frequency, & route used*	*Therapy Dates*
KLONOPIN (CLONAZEPAM)	0.5 mg 1x per 1 Day, Oral	06/00/2000 to Continues
IRON (IRON)	325 mg 1x per 1 Day, Oral	01/00/1999 to Continues
CEFTIN (CEFUROXIME AXETIL)	unknown, Oral	unknown
SINEQUAN (DOXEPIN HYDROCHLORIDE)	10 mg given as needed, Oral	Continues

DSS

FEB 0 9 2001

[redacted]

Individual Safety Report

3665982-4-00-01

MEDWATCH

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

VOLUNTARY reporting by health professionals of adverse events and product problems

Internet Submission - Page 1

Form Approved: OMB No. 0910-0291 Expires: 12/31/00
See OMB statement on reverse.

FDA Use Only

Triage unit sequence # 137689

A. Patient information

1. Patient identifier	2. Age at time of event:	3. Sex	4. Weight
5/200 case #14 In confidence	60 Years or Date of birth:	☐ female ☑ male	____ lbs or ____ kgs

B. Adverse event or product problem

1. ☑ **Adverse event** and/or ☐ **Product problem** (e.g., defects/malfunctions)

2. **Outcomes attributed to adverse event** (check all that apply)
- ☐ death (mm/dd/yyyy)
- ☐ life-threatening
- ☑ hospitalization – initial or prolonged
- ☐ disability
- ☐ congenital anomaly
- ☐ required intervention to prevent permanent impairment/damage
- ☐ other

3. **Date of event** (mm/dd/yyyy): 06/07/2000

4. **Date of this report** (mm/dd/yyyy): 02/13/2001

5. **Describe event or problem**

60yo presented with malaise/fatigue and dark tarry stool for 1 day. Prior to hydration Hct 27%. Pt took 2 Advils for shoulder pain the day prior to admission. Hct dropped to 22 and transfused 2 u PRBC. No further bleeding after admission

6. **Relevant tests/laboratory data**, including dates

7. **Other relevant history, including preexisting medical conditions** (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction etc.)

CTV137689

C. Suspect medication(s)

1. **Name** (Procuct Name) / (Labeled Strength) / (Mfr/Labeler)
- #1 Advil
- #2

2. **Dose/Frequency/Route used**
- #1
- #2

3. **Therapy dates** (if unknown, give duration)
- #1 From – To (or best est mate)
- #2 From – To (or best est mate)

4. **Diagnosis for use** (separate indications with commas)
- #1 pain relief
- #2

5. **Event abated after use stopped or dose reduced**
- #1 ☐ yes ☐ no ☐ doesn't apply
- #2 ☐ yes ☐ no ☐ doesn't apply

6. **Lot #** (if known)
- #1
- #2

7. **Exp. date** (if known)
- #1
- #2

8. **Event reappeared after reintroduction**
- #1 ☐ yes ☐ no ☐ doesn't apply
- #2 ☐ yes ☐ no ☐ doesn't apply

9. **NDC #** (for product problems only)
- –
- –

10. **Concomitant medical products** and therapy dates (exclude treatment of event)

D. Suspect medical device

1. **Brand name**

2. **Type of device**

3. **Manufacturer name & address**

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FEB 15 2001

4. **Operator of device**
- ☐ health professional
- ☐ lay user/patient
- ☐ other:

5. **Expiration date** (mm/dd/yyyy)

6.
- **model #** MEDWATCH CTU
- **catalog #**
- **serial #**
- **lot #**
- **other #**

7. **If implanted, give date** (mm/dd/yyyy)

8. **If explanted, give date** (mm/dd/yyyy)

9. **Device available for evaluation?** (Do not send device to FDA)
☐ yes ☐ no ☐ returned to manufacturer on (mm/dd/yyyy)

10. **Concomitant medical products** and therapy dates (exclude treatment of event)

E. Reporter (see confidentiality section on back)

1. **Name** [redacted] **phone #** [redacted]

[redacted] VAMC 50 IrvingStreet N.W
Washington District of Columbia 20422
United States [redacted] Med.VA.Gov

FEB 15 2001

2. **Health professional?** ☑ yes ☐ no

3. **Occupation** Pharmacist

4. **Also reported to**
- ☐ manufacturer
- ☐ user facility
- ☐ distributor

5. **If you do not want your identity disclosed to the manufacturer, place an "X" in this box.** ☐

FDA

Mail to: MEDWATCH, 5600 Fishers Lane, Rockville, MD 20852-9787 or FAX to: 1-800-FDA-0178

FDA Form 3500

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

Individual Safety Report

3666006-5-00-01

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

VOLUNTARY reporting
ealth professionals of adverse
ents and product problems

Page ___ of ___

Form Approved: OMB No. 0910-0291 Expires: 12/3
See OMB statement on reve

FDA Use Only

Triage unit sequence # 137675

A. Patient information

1. Patient identifier: 5757 (In confidence)
2. Age at time of event: 27 or Date of birth:
3. Sex: ☐ female ☐ male
4. Weight: ___ lbs or ___ kgs

B. Adverse event or product problem

1. ☒ Adverse event and/or ☐ Product problem (e.g., defects/malfunctions)
2. Outcomes attributed to adverse event (check all that apply)
   - ☐ death ___ (mo/day/yr)
   - ☐ life-threatening
   - ☒ hospitalization – initial or prolonged
   - ☐ disability
   - ☐ congenital anomaly
   - ☐ required intervention to prevent permanent impairment/damage
   - ☐ other:
3. Date of event (mo/day/yr): 11-1-06
4. Date of this report (mo/day/yr):
5. Describe event or problem

HEMATEMESIS +

MYLANTA X 3 DAYS

6. Relevant tests/laboratory data, including dates

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction etc.)

CTV137675

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
   #1 IBUPROFEN (OTC)
   #2
2. Dose, frequency & route used
   #1 N/A
   #2
3. Therapy dates (if unknown, give duration) from/to (or best estimate)
   #1 N/A
   #2
4. Diagnosis for use (indication)
   #1 PAIN
   #2
5. Event abated after use stopped or dose reduced
   #1 ☒ yes ☐ no ☐ does not apply
   #2 ☐ yes ☐ no ☐ does not apply
6. Lot # (if known)
   #1
   #2
7. Exp. date (if known)
   #1
   #2
8. Event reappeared after reintroduction
   #1 ☐ yes ☐ no ☒ does not apply
   #2 ☐ yes ☐ no ☐ does not apply
9. NDC # (for product problems only)
   - -
10. Concomitant medical products and therapy dates (exclude treatment of event)
    RANITIDINE

D. Suspect medical device

1. Brand name
2. Type of device
3. Manufacturer name & address

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4. Operator of device
   - ☐ health professional
   - ☐ lay user/patient
   - ☐ other:
5. Expiration date (mo/day/yr)
6. model # MEDWATCH CTU
   catalog #
   serial #
   lot #
   other #
7. If implanted, give date (mo/day/yr)
8. If explanted, give date (mo/day/yr)
9. Device available for evaluation? (Do not send to FDA)
   ☐ yes ☐ no ☐ returned to manufacturer on ___ (mo/day/yr)
10. Concomitant medical products and therapy dates (exclude treatment of event)

E. Reporter (see confidentiality section on back)

1. Name, address & phone #

OVERTON BROOKS VA MEDICAL CENTER
510 EAST STONER AVENUE
SHREVEPORT,LOUISIANA 71101-4295
(318)-424-6001

DSS
FEB 15 2007

2. Health professional? ☒ yes ☐ no
3. Occupation: RPL
4. Also reported to
   - ☐ manufacturer
   - ☐ user facility
   - ☐ distributor
5. If you do NOT want your identity disclosed to the manufacturer, place an " X " in this box. ☒

FDA

Mail to: MEDWATCH
5600 Fishers Lane
Rockville, MD 20852-9787

or FAX to:
1-800-FDA-0178

FDA Form 3500 (6/93)

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

Individual Safety Report

3674580-8-00-01

MEDWATCH

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

VOLUNTARY reporting by health professionals of adverse events and product problems

Internet Submission - Page 1

Form Approved: OMB No. 0910-0291 Expires: 12/31/00
See OMB statement on reverse

FDA Use Only

Triage unit sequence # 138777

A. Patient information

1. Patient identifier: 1606 (In confidence)
2. Age at time of event: 77 Years or Date of birth:
3. Sex: [x] female [ ] male
4. Weight: ____ lbs or ____ kgs

B. Adverse event or product problem

1. [x] Adverse event and/or [ ] Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)
- [ ] death (mm/dd/yyyy)
- [ ] life-threatening
- [ ] hospitalization – initial or prolonged
- [ ] disability
- [ ] congenital anomaly
- [x] required intervention to prevent permanent impairment/damage
- [ ] other:

3. Date of event (mm/dd/yyyy): 01/29/2001

4. Date of this report (mm/dd/yyyy): 03/05/2001

5. Describe event or problem

Acute renal failure, gastrointestinal bleeding

6. Relevant tests/laboratory data, including dates

Creatinine clearance < 10 ml/min

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MAR 0 6 2001
MEDWATCH CTU

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

MEDWATCH
MAR 0 6 2001
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CTU 138777

C. Suspect medication(s)

1. Name (Product Name) / (Labeled Strength) / (Mfr/Labeler)
- #1 Ibuprofen / 200 mg /
- #2 BC Powder -aspirin- / 500 mg /

2. Dose/Frequency/Route used
- #1 200 mg / q4-6 hours / Oral
- #2 unknown / / Oral

3. Therapy dates (if unknown, give duration) From / To (or best estimate)
- #1 01/22/2001 - 01/29/2001
- #2 -

4. Diagnosis for use (separate indications with commas)
- #1 Headache
- #2

5. Event abated after use stopped or dose reduced
- #1 [x] yes [ ] no [ ] doesn apply
- #2 [x] yes [ ] no [ ] doesn apply

6. Lot # (if known)
- #1
- #2

7. Exp. date (if known)
- #1
- #2

8. Event reappeared after reintroduction
- #1 [ ] yes [ ] no [x] doesn apply
- #2 [ ] yes [ ] no [x] doesn apply

9. NDC # (for product problems only)
- -
- -

10. Concomitant medical products and therapy dates (exclude treatment of event)

D. Suspect medical device

1. Brand name

2. Type of device

3. Manufacturer name & address

4. Operator of device
- [ ] health professional
- [ ] lay user/patient
- [ ] other:

5. Expiration date (mm/dd/yyyy)

6
- model # DSS
- catalog #
- serial # MAR 0 6 2001
- lot #
- other #

7. If implanted, give date (mm/dd/yyyy)

8. If explanted, give date (mm/dd/yyyy)

9. Device available for evaluation? (Do not send device to FDA)
[ ] yes [ ] no [ ] returned to manufacturer on ____ (mm/dd/yyyy)

10. Concomitant medical products and therapy dates (exclude treatment of event)

E. Reporter (see confidentiality section on back)

1. Name: [redacted] Pharm.D.
[redacted] Ave.
[redacted] United States [redacted]

phone #: [redacted]

2. Health professional? [x] yes [ ] no

3. Occupation: Pharmacist

4. Also reported to
- [ ] manufacturer
- [x] user facility
- [ ] distributor

5. If you do not want your identity disclosed to the manufacturer, place an "X" in this box. [x]

FDA

Mail to: MEDWATCH, 5600 Fishers Lane, Rockville, MD 20852-9787 or FAX to: 1-800-FDA-0178

FDA Form 3500

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

Individual Safety Report — VOLUNTARY reporting professionals of adverse and product problems

THI *3681966-4-00-01*

Form Approved: OMB No. 0910-0291 Expires: 12/31/01
See OMB statement on reverse.

FDA Use Only
Triage unit sequence # 139335

A. Patient information

1. Patient identifier	2. Age at time of event: / Date of birth:	3. Sex	4. Weight
16578Y In confidence	30	☒ female ☐ male	____ lbs or ____ kgs

B. Adverse event or product problem

1. ☒ Adverse event and/or ☐ Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)
- ☐ death ____ (mo/day/yr)
- ☐ life-threatening
- ☐ hospitalization – initial or prolonged
- ☐ disability
- ☐ congenital anomaly
- ☐ required intervention to prevent permanent impairment/damage
- ☐ other: ____

3. Date of event (mo/day/yr)	4. Date of this report (mo/day/yr)
1-4-01	3-15-01

5. Describe event or problem
admitted Tam ER c GI Bleed.

6. Relevant tests/laboratory data, including dates
D/C advil; began Prevacid gave 2 units PRBC's

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)
anemia
NKA.

MAR 16 2001

CTV139335

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
#1 advil
#2

2. Dose, frequency & route used	3. Therapy dates (if unknown, give duration) (mo/yr to (or best estimate))
#1 600mg tid	#1 ?
#2	#2

4. Diagnosis for use (indication)	5. Event abated after use stopped or dose reduced
#1 Pain	#1 ☒ yes ☐ no ☐ doesn't apply
#2	#2 ☐ yes ☐ no ☒ doesn't apply

6. Lot # (if known)	7. Exp. date (if known)	8. Event reappeared after reintroduction
#1	#1	#1 ☐ yes ☐ no ☐ doesn't apply
#2	#2	#2 ☐ yes ☐ no ☐ doesn't apply

9. NDC # (for product problems only)
- –

10. Concomitant medical products and therapy dates (exclude treatment of event)
—

D. Suspect medical device

1. Brand name
2. Type of device
3. Manufacturer name & address

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4. Operator of device
- ☐ health professional
- ☐ lay user/patient
- ☐ other: ____

6. Expiration date (mo/day/yr)

model # ____
catalog # ____
serial # ____
lot # ____
other # ____

7. If implanted, give date (mo/day/yr)
8. If explanted, give date (mo/day/yr)

9. Device available for evaluation? (Do not send to FDA)
☐ yes ☐ no ☐ returned to manufacturer on ____ (mo/day/yr)

10. Concomitant medical products and therapy dates (exclude treatment of event)

E. Reporter (see confidentiality section on back)

1. Name, address & phone #
[redacted]
DSS
Center
MAR 16 2001

2. Health professional?	3. Occupation	4. Also reported to
☒ yes ☐ no	pharmacist	☐ manufacturer ☐ user facility ☐ distributor

5. If you do NOT want your identity disclosed to the manufacturer, place an " X " in this box. ☒

FDA Mail to: MEDWATCH, 5600 Fishers Lane, Rockville, MD 20852-9787 or FAX to: 1-800-FDA-0178

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event

Individual Safety Report
3702992-2-00-01

MEDWATCH
THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

VOLUNTARY reporting
by health professionals of adverse events and product problems

Page ___ of ___

CDER

FDA Use Only
Triage unit sequence # 140922

I. Patient information
1. Patient identifier (In confidence)
2. Age at time of event: 80 or Date of birth:
3. Sex: ☐ female ☒ male
4. Weight: ___ lbs or 73 kgs

B. Adverse event or product problem
1. ☒ Adverse event and/or ☐ Product problem (e.g., defects/malfunctions)
2. Outcomes attributed to adverse event (check all that apply)
☐ death ___ (mm/dd/yyyy)
☒ life-threatening
☒ hospitalization – initial or prolonged
☐ disability
☐ congenital anomaly
☒ required intervention to prevent permanent impairment/damage
☐ other: ___
3. Date of event (mm/dd/yyyy): 3/14/2001
4. Date of this report (mm/dd/yyyy): 4/10/2001
5. Describe event or problem

Pt taking Coumadin at home for atrial fibrillation and Advil for "flu like symptoms." Admitted to the hospital to the intensive care unit for a GI bleed. Pt received Vitamin K 10mg x2 and FFP on admit. Spent 3days in the ICU, then transferred to the floor. Pt D/ced after 5days.

6. Relevant tests/laboratory data, including dates

	3/14	3/15 (06)	3/15 (11)	3/15 (20)	3/16 (04)	3/16 (12)	3/17
HGB	10.0	8.1	8.4	9.4	7.2	8.7	8.0
HCT	29.0	23.5	24.6	27.2	20.8	24.6	22.9
PLTS	186	146	123	140	124	114	120
BUN	78	78	—	—	—	—	29
Scr	1.2	0.9	—	—	1.8	—	0.8
PT	22.0	—	19.6	—	17.8	—	15.6
INR	3.3	3.4	2.6	—	2.0	—	1.6
K+	3.4	—	—	—	3.9	—	4.0
dig	0.8	—	—	—	—	—	—

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

NKA
Prostate CA
Asthma
A. fib
HTN
Radiation cystitis

APR 10 2001

CTV140922

C. Suspect medication(s)
1. Name (give labeled strength & mfr/labeler, if known)
#1 Warfarin (Coumadin®)
#2 ibuprofen (Advil®) 200mg tab
2. Dose, frequency & route used
#1
#2
3. Therapy dates (if unknown, give duration)
#1 PTA
#2 PTA
4. Diagnosis for use (indication)
#1 atrial fibrillation
#2 flu
5. Event abated after use stopped or dose reduced
#1 ☒ yes ☐ no ☐ doesn't apply
#2 ☒ yes ☐ no ☐ doesn't apply
6. Lot # (if known)
#1
#2
7. Exp. date (if known)
#1
#2
8. Event reappeared after reintroduction
#1 ☐ yes ☐ no ☒ doesn't apply
#2 ☐ yes ☐ no ☒ doesn't apply
9. NDC # (for product problems only)
10. Concomitant medical products and therapy dates (exclude treatment of event)
Zestril + Coreg + digoxin

D. Suspect medical device
1. Brand name
2. Type of device
3. Manufacturer name & address

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APR 11 2001
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4. Operator of device
☐ health professional
☐ lay user/patient
☐ other: ___
5. Expiration date (mm/dd/yyyy)
6. model # ___ catalog # ___ serial # ___ lot # ___ other # ___
7. If implanted, give date (mm/dd/yyyy)
8. If explanted, give date (mm/dd/yyyy)
9. Device available for evaluation? (Do not send to FDA)
☐ yes ☐ no ☐ returned to manufacturer on ___ (mm/dd/yyyy)
10. Concomitant medical products and therapy dates (exclude treatment of event)

E. Reporter (see confidentiality section on back)
1. Name, address & phone #
[redacted], Pharm D
[redacted] Hospital Pharmacy
[redacted]
2. Health professional? ☒ yes ☐ no
3. Occupation: Pharmacist
4. Also reported to
☐ manufacturer
☐ user facility
☐ distributor
5. If you do NOT want your identity disclosed to the manufacturer, place an "X" in this box. ☐

530

FDA Mail to: MEDWATCH 5600 Fishers Lane or FAX to: 1-800-FDA-0178

Individual Safety Report

3717534-5-00-01

OLUNTARY reporting
lth professionals of adverse
its and product problems

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

Internet Submission - Page 1

Form Approved: OMB No. 0910-0291 Expires: 04/: 003
See OMB statement on reverse

FDA Use Only

Triage unit sequence # 142688

A. Patient information

1. Patient identifier	2. Age at time of event: / Date of birth:	3. Sex	4. Weight
7285 In confidence	50 Years or _____	☐ female ☑ male	_____ lbs or 86 kgs

B. Adverse event or product problem

1. ☑ Adverse event and/or ☐ Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)
- ☐ death _____ (mm/dd/yyyy)
- ☐ life-threatening
- ☑ hospitalization – initial or prolonged
- ☐ disability
- ☐ congenital anomaly
- ☑ required intervention to prevent permanent impairment/damage
- ☐ other: _____

3. Date of event: 04/11/2001 (mm/dd/yyyy)

4. Date of this report: 05/03/2001 (mm/dd/yyyy)

5. Describe event or problem

Admitted with GIB and erosive eosaphagitis. Also with AVN, cataracts, and HTN associated with chronic steroid use.

MAY 0 4 2001

6. Relevant tests/laboratory data, including dates

Chem7 141/4.2/107/22/31/1.1/102 CBC 11.3/21.8/292 MCV 84.3

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

1. Asthma 2. R THA due to AVN 3. Bilat. cataracts 4. HTN

CTV142688 MAY 0 4 2001

C. Suspect medication(s)

1. Name (Product Name)	(Labeled Strength)	(Mfr/Labeler)
#1 Ibuprofen	200mg	Unknown OTC
#2 Prednisone	5mg	

2. Dose/Frequency/Route used	3. Therapy dates (if unknown, give duration) From / To (or best estimate)
#1 200mg / Unknown / Oral	#1 03/10/2001 - 04/11/2001
#2 Varies / qD / Oral	#2 02/02/1994 - 05/03/2001

4. Diagnosis for use (separate indications with commas)
#1 Hip Pain, self-medicating.
#2 Asthma

5. Event abated after use stopped or dose reduced
#1 ☑ yes ☐ no ☐ doesn't apply
#2 ☐ yes ☐ no ☑ doesn't apply

6. Lot # (if known)
#1
#2

7. Exp. date (if known)
#1
#2

8. Event reappeared after reintroduction
#1 ☐ yes ☐ no ☑ doesn't apply
#2 ☐ yes ☐ no ☐ doesn't apply

9. NDC # (for product problems only)
– –

10. Concomitant medical products and therapy dates (exclude treatment of event)

D. Suspect medical device

1. Brand name

2. Type of device

3. Manufacturer name & address

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MAY 0 4 2001

4. Operator of device
- ☐ health professional
- ☐ lay user/patient
- ☐ other: _____

6. model # _____
catalog # MEDWATCH CTU
serial # _____
lot # _____
other # _____

5. Expiration date (mm/dd/yy)

7. If implanted, give date (mm/dd/yy)

8. If explanted, give date (mm/dd/yyyy)

9. Device available for evaluation? (Do not send device to FDA)
☐ yes ☐ no ☐ returned to manufacturer on _____ (mm/dd/yyyy)

10. Concomitant medical products and therapy dates (exclude treatment of event)

E. Reporter (see confidentiality section on back)

1. Name [redacted], PharmD
VA PSHCS, 1660 S. Columbian Way
Seattle Washington 98108
United States [redacted]@med.va.gov

phone # [redacted]

2. Health professional? ☑ yes ☐ no

3. Occupation: Pharmacist

4. Also reported to
- ☐ manufacturer
- ☐ user facility
- ☐ distributor

5. If you do not want your identity disclosed to the manufacturer, place an "X" in this box. ☑

FDA

Mail to: MEDWATCH
5600 Fishers Lane
Rockville, MD 20852-9787

or FAX to: 1-800-FDA-0178

FDA Form 3500

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

TM
WYET
BOX 8:
PHILADELPHIA, PA 19101

Individual Safety Report
3721030-9-00-01

VATCH
OTS REPORTING PROGRAM

Approved by the FDA on 09/24/1999

Mfr report # HQ6558130JAN2001

UF Dist report #

FDA Use Only

A. Patient information

1. Patient identifier	2. Age at time of event: or Date of Birth:	3. Sex	4. Weight
[redacted] in confidence	15Yr	[X] female [ ] male	UNK lbs or kgs

B. Adverse event or product problem

1. [X] Adverse event [ ] Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)

- [ ] death (mo/day/yr)
- [ ] life-threatening
- [ ] hospitalization - initial or prolonged
- [X] recovered
- [ ] disability
- [ ] congenital anomaly
- [ ] required intervention to prevent permanent impairment/damage
- [ ] other:

3. Date of event (mo/day/yr): UNK

4. Date of this report (mo/day/yr): 05/08/2001

5. Describe event or problem

Information was received on 26-JAN-2001 from a Healthcare Professional concerning his white 15 year old daughter who had taken two ADVIL (IBUPROFEN) (Capsule, Liquid Filled) capsules (therapy dates unknown). The reporter stated his daughter has no history of Gastrointestinal or rectal disorders and was not taking concomitant drug therapy. The daughter experienced red blood in her stool (Melena) on an unknown date. According to the reporter, while on vacation with his family in Pakistan, his daughter noted "fresh blood" in her stool approximately one day after taking two liquigels for headache symptom relief. The reporter clarified "fresh blood" to mean "red colored blood, not black or brown colored blood." He advised his daugher to discontinue using the product and no blood was noted in subsequent stools. The reporter stated his daughter had used ADVIL in the past for headache and pain relief with no event. Reporter noted that in general he encouraged his daughter to take ADVIL (IBUPROFEN) only

(cont'd)

6. Relevant tests/laboratory data, including dates

None Provided.

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

UNK

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)

#1 ADVIL (IBUPROFEN, Capsule, Liquid Filled)

#2

2. Dose, frequency & route used

#1 2 liquigels as needed, Oral

#2

3. Therapy dates (if unknown, give duration)

#1 Not specified

#2

4. Diagnosis for use (indication)

#1 Headache NOS

#2

5. Event abated after use stopped or dose reduced

#1 [X] yes [ ] no [ ] doesn't apply

#2 [ ] yes [ ] no [ ] doesn't apply

6. Lot # (if known)

#1

#2

7. Exp date (if known)

#1

#2

8. Event reappeared after reintroduction

#1 [ ] yes [ ] no [X] doesn't apply

#2 [ ] yes [ ] no [ ] doesn't apply

9. NDC # - for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)

UNK

G. All manufacturers

1. Contact office - name/address

WHITEHALL-ROBINS
201 King of Prussia
Sixth Floor
Radnor, PA 19087-5114

Jill Robinson

2. Phone number: 6109644680

3. Report source (check all that apply)

- [ ] foreign
- [ ] study
- [ ] literature
- [ ] consumer
- [X] health professional
- [ ] user facility
- [ ] company representative
- [ ] distributor
- [ ] other:

4. Date received by manufacturer (mo/day/yr): 01/26/2001

5. (A)NDA 20-402
IND #
PLA #
pre-1938 [ ] yes
OTC product [X] yes

6. If IND, protocol #

7. Type of report

- [ ] 5-day
- [ ] 15-day
- [ ] 10-day
- [X] periodic
- [X] initial
- [ ] follow-up #

8. Adverse event term(s)

Melena

9. Mfr. report number

HQ6558130JAN2001

E. Initial reporter

1. Name & address: [redacted] Dr. [redacted] US phone # [redacted]

2. Health professional? [X] yes [ ] no

3. Occupation: Pediatrician

4. Initial reporter also sent report to FDA: [ ] yes [ ] no [X] unk

WYETH
BOX 82
PHILADELPHIA, PA 19101

Individual Safety Report
3721030-9-00-02

'ATCH
:TS REPORTING PROGRAM

Approved by the FDA on 09/24/1999

Mfr report # HQ6583130JAN2001

UF/Dist report #

FDA Use Only

Box 5.) - Describe event or problem (Continuation)

with food and not for an empty stomach. Reporter also stated he felt the blood may have been due to changes in diet while in Pakistan, but since another family member reported experiencing the same problem (the reporter's mother-in- law), he felt he should notify the manufacturer. Reporter was using sample packs while in Pakistan and did not return to the United States with any, nor did he recall the lot number associated with the samples.

TM WYETH-AY
BOX 8299
PHILADELPHIA, PA 19101

Individual Safety Report
3721033-4-00-01

TCH
REPORTING PROGRAM

Approved by the FDA on 09/24/1999

Mfr report # HQ6839405FEB2001

UF/Dist report #

FDA Use Only

A. Patient information

1. Patient identifier	2. Age at time of event	3. Sex	4. Weight
[redacted]	or 49Yr	[X] female	104 lbs
In confidence	Date of Birth	[ ] male	or kgs

B. Adverse event or product problem

1. [X] Adverse event [ ] Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)

- [ ] death (mo/day/yr)
- [ ] life-threatening
- [ ] hospitalization–initial or prolonged
- [X] recovered
- [ ] disability
- [ ] congenital anomaly
- [ ] required intervention to prevent permanent impairment/damage
- [ ] other:

3. Date of event (mo/day/yr): 01/15/2001

4. Date of this report (mo/day/yr): 05/08/2001

5. Describe event or problem

Information has been received on 31-JAN-2001 from a 49-year-old, white, female consumer. The patient's concurrent illnesses included insomnia, neck pain, and shoulder pain. Concomitant therapy included PREMPRO (CONJUGATED ESTROGENS/MEDROXYPROGESTERONE ACETATE) and DALMANE (FLURAZEPAM HYDROCHLORIDE). Therapy with ADVIL (IBUPROFEN) (Capsule, Liquid Filled) for shoulder and neck pain began at an unknown date and ceased on 18-JAN-2001. The dosage regimen included 6-7 liqui-gel caps by mouth daily as needed. Additional suspect medication included ADVIL (IBUPROFEN) (Caplet), which the patient administered 2-4 caplets by mouth daily for 10 years prior to switching to Advil Liquid Capsule. The patient experienced stomach pain (Abdominal pain upper) starting on 15-JAN-2001. Her physician stated that she had an ulcer (Gastrointestinal ulcer NOS) on 18-JAN-2001. The physician prescribed PRILOSEC as the treatment drug. At the time of the report the patient had recovered. Additional information has been

(cont'd)

6. Relevant tests/laboratory data, including dates

None Provided.

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

CONCURRENT CONDITIONS:
Arthralgia, Insomnia NEC; Neck pain

C. Suspect medication(s)

1. Name (give strength & manufacturer, if known)

#1 ADVIL (IBUPROFEN, Capsule, Liquid Filled)

#2

(cont'd)

2. Dose, frequency & route used

#1 6-7 liqui-gel caps daily as needed, Oral

#2

3. Therapy dates (if unknown, give duration)

#1 UNK to 01/18/2001

#2

4. Diagnosis for use (indication)

#1 Arthralgia, Neck pain. Arthralgia, Neck pain

#2

5. Event abated after use stopped or dose reduced

#1 [ ] yes [ ] no [ ] doesn't apply UNK

#2 [ ] yes [ ] no [ ] doesn't apply

6. Lot # (if known)

#1 3001667, 3001930

#2

7. Exp date (if known)

#1

#2

8. Event reappeared after reintroduction

#1 [ ] yes [ ] no [X] doesn't apply

#2 [ ] yes [ ] no [ ] doesn't apply

9. NDC # – for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)

See following Page.

G. All manufacturers

1. Contact office – name/address

WHITEHALL-ROBINS
201 King of Prussia
Sixth Floor
Radnor, PA 19087-5114

Jill Robinson

2. Phone number: 6109644680

3. Report source (check all that apply)

- [ ] foreign
- [ ] study
- [ ] literature
- [X] consumer
- [ ] health professional
- [ ] user facility
- [ ] company representative
- [ ] distributor
- [ ] other:

4. Date received by manufacturer (mo/day/yr): 01/31/2001

5. (A)NDA 20-402
IND #
PLA #
pre-1938 [ ] yes
OTC product [X] yes

6. If IND, protocol #

7. Type of report

- [ ] 5-day
- [ ] 15-day
- [ ] 10-day
- [X] periodic
- [X] initial
- [ ] follow-up #

8. Adverse event term(s)

Gastrointestinal ulcer NOS
Abdominal pain upper

9. Mfr. report number: HQ6838405FEB2001

E. Initial reporter

1. Name & address

[redacted] Ms.
[redacted] DE, [redacted] US

phone # [redacted]

2. Health professional? [ ] yes [X] no

3. Occupation: UNK

4. Initial reporter also sent report to FDA [ ] yes [ ] no [X] unk

FDA Form 3500A (facsimile)

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

TM
WYETH-A
BOX 8299
PHILADELPHIA, PA 19101

Individual Safety Report

3721033-4-00-02

ATCH

REPORTING PROGRAM

Approved by the FDA on 09/24/1999

Mfr report # HQ5838405FBS2001

UF/Dist report #

FDA Use Only

Box B.5 - Describe event or problem (Continuation)

requested.

Box C - Suspect medication(s) (Continuation)

1. Name (give labeled strength & mfr/labeler, if known)

1.2 ADVIL (IBUPROFEN, Caplet)

2. Dose, frequency & route used

1.2 1-4 caplets daily as needed, Oral

3. Therapy dates (if unknown, give duration)

1.2 00/00/1991 to UNK

6. Lot # (if known)

7. Exp date (if known)

Box C.10 - Concomitant medical products and therapy dates (exclude treatment of event) (Continuation)

Therapy Name	*Dose, frequency, & route used*	*Therapy Dates*
DALMANE (FLURAZEPAM HYDROCHLORIDE)	15 mg 1x per 1 Wk, Oral	unknown Continues
PREMPRO (CONJUGATED ESTROGENS/MEDROXYPROGESTERONE ACETATE)	"(0.625mg)" daily, Oral	00/00/1998 to Continues

Individual Safety Report

3722030-5-00-01

nan Health Division

use by user-facilities,
ors and manufacturers for
NDATORY reporting

Page 1

50325904

Merck Facsimile of FDA Form 3500A
Approved by FDA (10/21/93)

Mfr report #	WAES 01050455
UF/Dist report #	
	FDA Use Only

NO ATTACHMENT

A. Patient information

1. Patient identifier	2. Age at time of event:	3. Sex	4. Weight
[redacted] in confidence	or 71 years Date of Birth: [redacted]	[X] Female [ ] Male	Unk

B. Adverse event or product problem

1. [X] Adverse event [ ] and / or [ ] Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)

- [ ] death (mo/day/yr) _____
- [X] life-threatening
- [X] hospitalization-initial or prolonged
- [ ] disability
- [ ] congenital anomaly
- [ ] required intervention to prevent permanent impairment/damage
- [X] other: important medical

3. Date of event (mo/day/yr)	4. Date of this report (mo/day/yr)
10/24/00	05/08/01

5. Describe event or problem

Information has been received from a pharmacist concerning a 71 year old female with hypertension, congestive heart failure, renal insufficiency, decreased calcium, a seizure disorder and depression and a history of a cerebrovascular accident who was placed on therapy with rofecoxib, tablet for the treatment of the pain of osteoporosis (dose and duration not reported). Concomitant therapy included alendronate sodium (MSD), tablet, for the treatment of osteoporosis (duration and dose not reported); ibuprofen (ADVIL), tablet, (dose, duration and indication unknown) and clopidogrel bisulfate (PLAVIX), tablet, for the treatment of a cerebrovascular accident (dose and duration unknown). Other concomitant therapy included diltiazem hydrochloride (TIAZAC), calcium (unspecified), lisinopril (ZESTRIL), sertraline HCl (ZOLOFT), potassium (unspecified) and hydrochlorothiazide (manufacturer unknown). On 24-OCT-2000 the patient developed a gastrointestinal bleed from "multiple meds" and was hospitalized. The pharmacist noted that the suspected therapies included rofecoxib, alendronate sodium (MSD).

(Continued on Additional Page)

6. Relevant tests/laboratory data, including dates

Unknown

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D MAY 11 2001 CDR

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

MEDICAL HISTORY: cerebrovascular accident
CONCURRENT CONDITIONS: congestive heart failure; depression; hypertension; hypocalcemia; renal insufficiency; seizure disorder

FDA Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)

#1 TAB VIOXX Unk
#2 TAB ADVIL Unk

(Continued on Additional Page)

2. Dose, frequency & route used	3. Therapy dates (from/to (if unknown, give duration)
#1 Unk/Unk/PO	#1 Unk - 10/24/00
#2 Unk/Unk/PO	#2 Unk - 10/24/00

4. Diagnosis for use (indication)

#1 pain, osteoporosis
#2 Unknown

5. Event abated after use stopped or dose reduced.

	yes	no	N/A	unk
#1	[X]	[ ]	[ ]	[ ]
#2	[X]	[ ]	[ ]	[ ]

6. Lot # (if known)	7. Exp date (if known)
#1	#1
#2	#2

8. Event reappeared after reintroduction

	yes	no	N/A	unk
#1	[ ]	[ ]	[X]	[ ]
#2	[ ]	[ ]	[X]	[ ]

9. NDC # - for product problems only (if known)

Unknown

10. Concomitant medical products and therapy dates (exclude treatment of event)

HYDRODIURIL	Unk -Unk
TIAZAC	Unk -Unk

(Continued on Additional Page)

G. All manufacturers

1. Contact office - name/address

Merck Human Health Division
Merck & Co., Inc.
P.O. Box 4
West Point, PA 19486-0004

ATTN: Worldwide Product Safety

2. Phone Number: (610)397-2416

3. Report source (check all that apply)

- [ ] foreign
- [ ] study
- [ ] literature
- [ ] consumer
- [X] health professional
- [ ] user facility
- [ ] company representative
- [ ] distributor
- [ ] other:

4. Date received by manufacturer (mo/day/yr): 05/03/01

5. (A)NDA # 21042
IND #
PLA #
pre-1938 [ ] yes
OTC product [ ] yes

6. If IND, protocol #

7. Type of report
[ ] 5-day [X] 15-day
[ ] 10-day [ ] periodic
[X] initial [ ] Follow-up# ____

9. Mfr report number: WAES 01050455

8. Adverse event term(s)

GASTROINTESTINAL BLEEDING

E. Initial reporter

1. Name, address & phone #

[redacted] HOSPITAL
DEPARTMENT OF PHARMACY
[redacted]

800-666-2648

DSS

MAY [illegible] 2001

2. Health professional?	3. Occupation	4. Initial reporter also sent report to FDA
[X] YES [ ] NO	Pharm.D.	[ ] yes [ ] no [X] unk

B. Advers

5. Describe event or problem

ibuprofen (ADVIL) and clopidogrel bisulfate (PLAVIX), and of these rofecoxib was the most likely suspect and alendronate sodium (MSD) was a "remote possibility." The patient was admitted to the intensive care unit and these "drugs" were discontinued. The patient was treated with intravenous famotidine (MSD) and transfused with packed red blood cells. Subsequently, the patient recovered.

Gastrointestinal bleed was considered to be immediately life-threatening and an other important medical event. Additional information is not expected.

The pharmacist also reported the experiences of other patients while on therapy with rofecoxib (WAES#'s 01020825, 01020826, 00022279, 00081100, 01050280).

C. Suspect medication(s)

1. Name (Given labeled strength & mfr/labeler, if known)

#3 TAB FOSAMAX Unk
#4 TAB PLAVIX Unk

2. Dose, frequency & route used

#3 Unk/Unk/PO
#4 Unk/Unk/PO

3. Therapy dates (from/to) (if unknown, give duration)

#3 Unk - 10/24/00
#4 Unk - 10/24/00

4. Diagnosis for use (indication)

#3 Unknown
#4 Unknown

5. Event abated after use stopped or dose reduced

	YES	NO	N/A	UNK
#3	X			
#4	X			

6. Lot # (if known)

#3
#4

7. Exp date (if known)

#3
#4

8. Event reappeared after reintroduction

	YES	NO	N/A	UNK
#3			X	
#4			X	

DSS

MAY 4 2001

C. Suspect medication(s)

10. Concomitant medical products and therapy dates (exclude treatment of event)

ZESTRIL	Unk	- Unk
ZOLOFT	Unk	- Unk
calcium (unspecified)	Unk	- Unk
potassium (unspecified)	Unk	- Unk

DSS

Individual Safety Report

3744946-6-00-01

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

OLUNTARY reporting
th professionals of adverse
ts and product problems

et Submission - Page 1

Form Approved: OMB No. 0910-0291 Expires: 04/30/03
See OMB statement on reverse

FDA Use Only

Triage unit sequence # 145986

A. Patient information

1. Patient identifier	2. Age at time of event: / or Date of birth:	3. Sex	4. Weight
[redacted] In confidence	79 Years	☑ female ☐ male	128 lbs or kgs

B. Adverse event or product problem

1. ☑ Adverse event and/or ☐ Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)
- ☐ death (mm/dd/yyyy)
- ☐ life-threatening
- ☑ hospitalization – initial or prolonged
- ☐ disability
- ☐ congenital anomaly
- ☐ required intervention to prevent permanent impairment/damage
- ☐ other:

3. Date of event: 04/07/2001 (mm/dd/yyyy)

4. Date of this report: 06/21/2001 (mm/dd/yyyy)

5. Describe event or problem

Patient was admitted with hematemesis, dizziness, and weakness. She had been taking ibuprofen 2 tablets every 6 hours for the past 2 months. On admission Hgb was 6.8. She recieved 2 units of PRBC. Patient underwent endoscopy that showed a 1 cm ulcer with a clot in the posterior wall of the lesser curve, a clot in the fundus, and a small ulcer in the antrum. Prilosec, Biaxin, Amoxicillin, and Tylenol prn were started for ulcer treatment.

6. Relevant tests/laboratory data, including dates

Hgb -on admission- 6.8 BP 120/58; Pulse 74; RR 13 Hgb -after a total of 4 units- 11.0 WBC 7,300 Plts 115,000 INR 1.4 H. pylori positive

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

No past medical history No alcohol use, non-smoker Meds on admission: ibuprofen NKDA Social hx: death of husband and brother, illness of son

C. Suspect medication(s)

1. Name (Product Name)	(Labeled Strength)	(Mfr/Labeler)
#1 ibuprofen -Advil-	200 mg	
#2		

2. Dose/Frequency/Route used	3. Therapy dates (if unknown, give duration) From / To (or best estimate)
#1 200 mg / Q6H / Oral	#1 02/01/2001 - 04/07/2001
#2	#2 -

4. Diagnosis for use (separate indications with commas)
#1
#2

5. Event abated after use stopped or dose reduced
#1 ☑ yes ☐ no ☐ doesn't apply
#2 ☐ yes ☐ no ☐ doesn't apply

6. Lot # (if known)	7. Exp. date (if known)
#1	#1
#2	#2

8. Event reappeared after reintroduction
#1 ☐ yes ☐ no ☐ doesn't apply
#2 ☐ yes ☐ no ☐ doesn't apply

9. NDC # (for product problems only)
- –

10. Concomitant medical products and therapy dates (exclude treatment of event)

D. Suspect medical device

1. Brand name

2. Type of device

3. Manufacturer name & address

4. Operator of device
- ☐ health professional
- ☐ lay user/patient
- ☐ other:

5. Expiration date (mm/dd/yyyy)

6.
model #
catalog #
serial #
lot #
other #

RECEIVED
JUN 25 2001
MEDWATCH CTU
DSS

7. If implanted, give date (mm/dd/yyyy)

8. If explanted, give date (mm/dd/yyyy)

9. Device available for evaluation (Do not send device to FDA)
☐ yes ☐ no ☐ returned to manufacturer on _____ (mm/dd/yyyy)

10. Concomitant medical products and therapy dates (exclude treatment of event)

JUN 25 2001

E. Reporter (see confidentiality section on back)

1. Name: [redacted] phone #: [redacted]
Pharm D Cand.
[redacted] Drug Information Services, [redacted]
[redacted] [redacted] [redacted]
United States

2. Health professional?	3. Occupation	4. Also reported to
☑ yes ☐ no	Pharmacist	☐ manufacturer ☑ user facility ☐ distributor

5. If you do not want your identity disclosed to the manufacturer, place an "X" in this box. ☐

FDA

Mail to: MEDWATCH, 5600 Fishers Lane, Rockville, MD 20852-9787 or FAX to: 1-800-FDA-0178

FDA Form 3500

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the eve nt.

CTU 145986

WYETH
Individual Safety Report

3749073-X-00-01

MEDWATCH

PRODUCTS REPORTING PROGRAM

Approved by the FDA on 09/24/1999

Mfr report # HQ2376421JUN2001

UF/Dist report #

FDA Use Only

A. Patient information

1. Patient identifier	2. Age at time of event:	3. Sex	4. Weight
UNKNOWN	or 39Yr	[ ] female	UNK lbs
in confidence	Date of Birth:	[X] male	or kgs

B. Adverse event or product problem

1. [X] Adverse event [ ] Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)

- [X] death (mo/day/yr)
- [ ] life-threatening
- [X] hospitalization–initial or prolonged
- [ ] recovered
- [ ] disability
- [ ] congenital anomaly
- [ ] required intervention to prevent permanent impairment/damage
- [ ] other:

3. Date of event (mo/day/yr)	4. Date of this report (mo/day/yr)
UNK	06/26/2001

5. Describe event or problem

Information was received on 20-JUN-2001 from a physician concerning a 39-year-old, male, patient. The patient's concurrent illnesses included chronic back pain. At the time of the adverse event it was reported by a family member that the patient had been a chronic alcohol drinker, and consumed 6 bottles of beer along with 6 bottles of wine coolers each evening. Therapy with Advil (ibuprofen) (tablet) for pain began and ended at unknown dates. The dosage regimen was 12 tablets daily at an unknown frequency (overdose NOS), which the physician termed, "chronic Advil abuse". Concomitant drug therapy included Pepcid (famotidine), Tums (calcium carbonate/magnesium carbonate/magnesium trisilicate), and Aspirin (acetylsalicylic acid). At an unknown date that patient was admitted to the emrgency room after experiencing abdominal pain (Abdominal pain NOS) and a "popping sensation" in the lower abdomen. The physician reported that the only significant clinical finding was gaurding in the right lower quadrant. Initial lab

(cont'd)

6. Relevant tests/laboratory data, including dates

See following page.

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

CONCURRENT CONDITIONS:
Back pain; Alcoholism; Drug abuse

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)

#1 ADVIL (IBUPROFEN, Tablet, 200 mg)

#2

2. Dose, frequency & route used (cont'd)	3. Therapy dates (if unknown, give duration)
#1 12 tablets daily (frequency unknown),	#1 unknown
#2	#2

4. Diagnosis for use (indication)	5. Event abated after use stopped or dose reduced
#1 Pain NOS	#1 [ ] yes [ ] no [X] doesn't apply
#2	#2 [ ] yes [ ] no [ ] doesn't apply

6. Lot # (if known)	7. Exp date (if known)	8. Event reappeared after reintroduction
#1	#1	#1 [ ] yes [ ] no [X] doesn't apply
#2	#2	#2 [ ] yes [ ] no [ ] doesn't apply

9. NDC # – for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)

See following Page.

G. All manufacturers

1. Contact office – name/address

WHITEHALL-ROBINS
201 King of Prussia
Sixth Floor
Radnor, PA 19087-5114

Jill Robinson

JUN 2 7

2. Phone number: 6109644680

3. Report source (check all that apply)

- [ ] foreign
- [ ] study
- [ ] literature
- [ ] consumer
- [X] health professional
- [ ] user facility
- [ ] company representative
- [ ] distributor
- [ ] other:

4. Date received by manufacturer (mo/day/yr): 06/20/2001

5. (A)NDA 18-989
IND #
PLA #
pre-1938 [ ] yes
OTC product [X] yes

6. If IND, protocol #

7. Type of report

- [ ] 5-day
- [X] 15-day
- [ ] 10-day
- [ ] periodic
- [X] initial
- [ ] follow-up #

8. Adverse event term(s)

Overdose NOS
Haematoma NOS
Respiratory arrest (neonatal)
Rectal bleeding
Abdominal pain NOS
Mouth haemorrhage

(cont'd)

JUN 27 2001

9. Mfr. report number: HQ2376421JUN2001

E. Initial reporter

1. Name & address

[redacted] Dr. [redacted] Road Suite [redacted] US

phone # [redacted]

DSS

JUN 28 2001

2. Health professional?	3. Occupation	4. Initial reporter also sent report to FDA
[X] yes [ ] no	UNK	[ ] yes [ ] no [X] unk

FDA Form 3500A (facsimile)

JUN 26 2001

DATE SENT TO FDA

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

WYETH
Individual Safety Report

3749073-X-00-02

MEDWATCH

PRODUCTS REPORTING PROGRAM

Approved by the FDA on 09/24/1999

Mfr report #	HQ2376421JUN2001
UF/Dist report #	
	FDA Use Only

Box B.5 - Describe event or problem (Continuation)

findings were WBC 16800 mm^3, Hgb 14.8 g/dL, and HCT 43.9%. An abdominal CT scan revealed right retroperitoneal phlegmon, which the radilologist stated could not be drained percutaneously. The patient was admitted and treated with IV fluids and broad spectrum antibiotics. The morning after the admission the patient went into respiratory arrest (respiratory arrest (exc neonatal)), and was intubated and transferred to an ICU. The patient had a nasogastric tube, foley catheter, and a triple lumen subclavian central catheter placed. The reporter stated, "The patient underwent an emergent exploratory laparotomy that day after stabilization. The operative finding was a right retroperitoneal hematoma (haematoma NOS), which extended from the duodenum to the pelvis. The retroperitoneal hematoma was not explored as it was not expanding and clotting studies were prolonged. Operative cultures were all negative. The patient was returned to the ICU where he developed progressive multisystem organ failure (multi-organ failure) including pulmonary, renal, and hepatic failure. He had diffuse bleeding from the mouth and anus (rectal bleeding) (mouth haemorrhage)." The physician also reported that all of the patient's clotting parameters were prolonged with a D-isomer level of >4.0. The patient received many units of blood, platelets, and fresh frozen plasma. The physician reported that the patient also received dialysis and went on to receive nutritional support. The patient died as a result of the adverse event two weeks after admission to the hospital.

Box B.6 - Relevant test/laboratory data, including dates (Continuation)

Test Name / *Date*	*Result*	*Normal Range*
Computerised tomogram abnormal		
	right retroperitoneal phlegmon	-
Haematocrit		
	43.9 %	-
Haemoglobin		
	14.8 g/dL	-
White blood cell count increased		
	16800 mm^3	-

Box C - Suspect medication(s) (Continuation from Lines #1 and #2 on original page)

2. Dose, frequency, & route used

1.1 Oral

Box C.10 - Concomitant medical products and therapy dates (exclude treatment of event) (Continuation)

Therapy Name	*Dose, frequency, & route used*	*Therapy Dates*
PEPCID (FAMOTIDINE)	unknown dose daily, Oral	unknown
TUMS (CALCIUM CARBONATE/MAGNESIUM CARBONATE/MAGNESIUM TRISILICATE)	unknown dose daily, Oral	unknown
ASPIRIN (ACETYLSALICYLIC ACID)	unknown dose daily, Oral	unknown

Box G.8 - Adverse event term(s) (Continuation)

Multi-organ failure

JUN 27 2001

DSS

JUN 28 2001

3760470-9-00-01

MEDWATCH

PRODUCTS REPORTING PROGRAM

Approved by the FDA on 09/24/1999

Mfr report # HQ9196631JUL2000

UF/Dist report #

FDA Use Only

A. Patient information

1. Patient identifier	2. Age at time of event:	3. Sex	4. Weight
UNKNOWN	or 53Yr	[X] female	165 lbs
in confidence	Date of Birth: [redacted]	[ ] male	or kgs

B. Adverse event or product problem

1. [X] Adverse event [ ] Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)

- [ ] death (mo/day/yr)
- [ ] life-threatening
- [X] hospitalization-initial or prolonged
- [X] recovered
- [ ] disability
- [ ] congenital anomaly
- [ ] required intervention to prevent permanent impairment/damage
- [ ] other:

3. Date of event (mo/day/yr): 10/00/1993

4. Date of this report (mo/day/yr): 07/16/2001

5. Describe event or problem

Information has been received on 28-JUL-2000 concerning a 53 Yr old White female patient who had taken ADVIL (Tablet) for Headache NOS. Therapy began in JUL-1993 and ceased in OCT-1993. The dose regimen included: 6 to 8 tablets daily. Concomitant therapy was not reported. The patient reported that her use of Advil resulted in perforated ulcers (Gastric ulcer perforation) in OCT-1993. The patient was hospitalized for 3 days in intensive care. Condition required 2 sugeries. Patient has recovered.

6. Relevant tests/laboratory data, including dates

None Provided.

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

UNK

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)

#1 ADVIL (IBUPROFEN, Tablet, Unspec)

#2

2. Dose, frequency & route used

#1 6 to 8 tablets daily, Oral

#2

3. Therapy dates (if unknown, give duration)

#1 07/00/1993 to 10/00/1993

#2

4. Diagnosis for use (indication)

#1 Headache NOS

#2

5. Event abated after use stopped or dose reduced

#1 [X] yes [ ] no [ ] doesn't apply

#2 [ ] yes [ ] no [ ] doesn't apply

6. Lot # (if known)

#1

#2

7. Exp date (if known)

#1

#2

8. Event reappeared after reintroduction

#1 [ ] yes [ ] no [X] doesn't apply

#2 [ ] yes [ ] no [ ] doesn't apply

9. NDC # - for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)

UNK

G. All manufacturers

1. Contact office - name/address

WHITEHALL-ROBINS
201 King of Prussia
Sixth Floor
Radnor, PA 19087-5114

Jill Robinson

2. Phone number: 6109644580

3. Report source (check all that apply)

- [ ] foreign
- [ ] study
- [ ] literature
- [X] consumer
- [ ] health professional
- [ ] user facility
- [ ] company representative
- [ ] distributor
- [ ] other:

4. Date received by manufacturer (mo/day/yr): 07/28/2000

5.
(A)NDA 18-980
IND #
PLA #
pre-1938 [ ] yes
OTC product [X] yes

6. If IND, protocol #

7. Type of report

- [ ] 5-day
- [ ] 15-day
- [ ] 10-day
- [X] periodic
- [X] initial
- [ ] follow-up #

8. Adverse event term(s)

Gastric ulcer perforation

9. Mfr. report number

HQ9196631JUL2000

E. Initial reporter

1. Name & address

[redacted] Ms.
US

phone #

JUL 17 2001

2. Health professional?
[ ] yes [X] no

3. Occupation
UNK

4. Initial reporter also sent report to FDA
[ ] yes [ ] no [X] unk

FDA Form 3500A (facsimile)

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

WYETH Safety Report

3760471-0-00-01

MEDWATCH

DUCTS REPORTING PROGRAM

Approved by the FDA on 09/24/1999

Mfr report # HQ9972420APR2001

UF/Dist report #

FDA Use Only

A. Patient information

1. Patient identifier	2. Age at time of event:	3. Sex	4. Weight
[redacted] confidence	or 42Yr Date of Birth:	[X] female [ ] male	UNK lbs or kgs

B. Adverse event or product problem

1 [X] Adverse event [ ] Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)

- [ ] death (mo/day/yr)
- [ ] life-threatening
- [X] hospitalization-initial or prolonged
- [X] recovered
- [ ] disability
- [ ] congenital anomaly
- [ ] required intervention to prevent permanent impairment/damage
- [ ] other:

3. Date of event (mo/day/yr): 04/12/2001

4. Date of this report (mo/day/yr): 07/16/2001

5. Describe event or problem

Information was received on 20-APR-2001 from a 42-year-old, white, female patient. The patient had a past medical history of a ruptured appendix, and melanoma. Therapy with Advil (ibuprofen) (tablet) for back pain began in APR-2000 and continued as needed for back pain until 12-APR-2001. The dosage regimen was 2 tablets by mouth daily. On 12-APR-2001 the patient had taken the product in the morning on an empty stomach, and subsequently drank a cup of coffee. The patient stated that she would occasionally take additional tablets after running for relief of back pain, which she did on 12-APR-2001. It was unknown if the patient was taking concomitant drug therapy. The patient experienced gastric ulcer perforation (gastric ulcer perforation), which began with vomitting blood and dark colored diarrhea-like stools on 12-APR-2001. The patient was taken to the emergency room, where she was diagnosed with gastric ulcer perforation. The ulcer was located above a blood vessel and was cauterized. The

(cont'd)

6. Relevant tests/laboratory data, including dates

None Provided.

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

PAST CONDITIONS:
Appendicitis perforated

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)

#1 ADVIL (IBUPROFEN, Tablet, 200 mg)

#2

2. Dose, frequency & route used

#1 2 Tablet 1x per 1 Day, Oral

#2

3. Therapy dates (if unknown, give duration)

#1 04/00/2000 to 04/12/2001

#2

4. Diagnosis for use (indication)

#1 Back pain

#2

5. Event abated after use stopped or dose reduced

#1 [X] yes [ ] no [ ] doesn't apply

#2 [ ] yes [ ] no [ ] doesn't apply

6. Lot # (if known)

#1

#2

7. Exp date (if known)

#1

#2

8. Event reappeared after reintroduction

#1 [ ] yes [ ] no [X] doesn't apply

#2 [ ] yes [ ] no [ ] doesn't apply

9. NDC # - for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)

UNK

G. All manufacturers

1. Contact office - name/address

WHITEHALL-ROBINS
201 King of Prussia
Sixth Floor
Radnor, PA 19087-5114

Jill Robinson

2. Phone number: 6109644680

3. Report source (check all that apply)

- [ ] foreign
- [ ] study
- [ ] literature
- [X] consumer
- [ ] health professional
- [ ] user facility
- [ ] company representative
- [ ] distributor
- [ ] other:

4. Date received by manufacturer (mo/day/yr): 04/20/2001

5. (A)NDA 18-989
IND #
PLA #
pre-1938 [ ] yes
OTC product [X] yes

6. If IND, protocol #

7. Type of report

- [ ] 5-day
- [ ] 15-day
- [ ] 10-day
- [X] periodic
- [X] initial
- [ ] follow-up #

8. Adverse event term(s)

Gastric ulcer perforation

9. Mfr. report number

HQ9972420APR2001

E. Initial reporter

1. Name & address

[redacted], Ms.
[redacted] Road
US

phone #

JUL 17 2001

2. Health professional? [ ] yes [X] no

3. Occupation: UNK

4. Initial reporter also sent report to FDA? [ ] yes [ ] no [X] unk

FDA Form 3500A (facsimile)

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

7

WYETH

3760471-0-00-02

MEDWATCH

DUCTS REPORTING PROGRAM

Approved by the FDA on 09/24/1999

Mfr report #	H2997420APR2001
UF/Dist report #	
	FDA Use Only

Box B.5 - Describe event or problem (Continuation)

patient reported that she had lost 1/3 of her total blood volume. The patient was discharged from the hospital in three days without sequelae, and had recovered at the time of the report.

JUL 17 2001

WYETH AYERST

MEDWATCH

RODUCTS REPORTING PROGRAM

Approved by the FDA on 09/24/1999

Individual Safety Report

3760817-3-00-01

Mfr report # HQ1081615FEB2000

UF/Dist report #

FDA Use Only

A. Patient information

1. Patient identifier	2. Age at time of event:	3. Sex	4. Weight
[redacted] 035	or 67Yr	[ ] female	UNK lbs
in confidence	Date of Birth: [redacted]	[X] male	or kgs

B. Adverse event or product problem

1. [X] Adverse event [ ] Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)

- [ ] death (mo/day/yr)
- [ ] life-threatening
- [X] hospitalization-initial or prolonged
- [X] recovered
- [ ] disability
- [ ] congenital anomaly
- [ ] required intervention to prevent permanent impairment/damage
- [ ] other:

3. Date of event (mo/day/yr): 01/23/2000

4. Date of this report (mo/day/yr): 07/16/2001

5. Describe event or problem

Information was received 4-FEB-2000, 11-FEB-2000, and 30-JUN-2000 from an investigator concerning a 67 year old male participant in a CR&D Study (RhBMP-2; protocol: C9730-11; investigator #772; patient #035). The patient's concurrent illness included dental implants (Tooth disorder NOS) placed on 11-JAN-2000. Additional medical history was not provided. Therapy with ADVIL (ibuprofen) Tablet for post-operative analgesia began on 13-JAN-2000 and ceased on 15-JAN-2000. The dose regimen included 3 tablets every day at bedtime. The product was then withdrawn. Additional suspect medication included recombinant human bone morphogenic protein-2 (RhBMP-2) implant (patient received 1.5 mg/ml rhBMP/ACS on 24-MAY-1999). Concomitant medications included CEPHALEXIN, DEXAMETHASONE, HYDROCODONE W/ACETAMINOPHEN, MEPERIDINE HYDROCHLORIDE, METHOHEXITAL, NITROUS OXIDE, PERIDEX, TETRACYCLINE, and XYLOCAINE . On 22-JAN-2000, the patient experienced abdominal pain and went to the Emergency Department. On 23-JAN-2000

(cont'd)

6. Relevant tests/laboratory data, including dates

See following page.

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

CONCURRENT CONDITIONS:
Tooth disorder NOS

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)

#1 ADVIL (IBUPROFEN, Tablet, Unspec)

#2 RECOMBINANT HUMAN BONE MORPHOGENETIC PROTEIN-2

2. Dose, frequency & route used	3. Therapy dates (if unknown, give duration)
#1 3 Tablet 1x per 1 Day, Oral	#1 01/13/2000 to 01/15/2000
#2 1.5 mg / ml ACS Surgical Implant, Other	#2 05/24/1999 to 05/24/1999

4. Diagnosis for use (indication)

#1 Post-operative analgesia

#2 Bone graft

5. Event abated after use stopped or dose reduced

#1 [ ] yes [ ] no [X] doesn't apply

#2 [ ] yes [ ] no [X] doesn't apply

6. Lot # (if known)

#1

#2118028AA

7. Exp date (if known)

#1

#2

8. Event reappeared after reintroduction

#1 [ ] yes [ ] no [X] doesn't apply

#2 [ ] yes [ ] no [X] doesn't apply

9. NDC # - for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)

See following Page.

G. All manufacturers

1. Contact office - name/address

WHITEHALL-ROBINS
201 King of Prussia
Sixth Floor
Radnor, PA 19087-5114

Jill Robinson

2. Phone number: 6109644680

3. Report source (check all that apply)

- [ ] foreign
- [ ] study
- [ ] literature
- [ ] consumer
- [X] health professional
- [ ] user facility
- [ ] company representative
- [ ] distributor
- [ ] other:

4. Date received by manufacturer (mo/day/yr): 06/30/2000

5. (A)NDA 18-989
IND #
PLA #
pre-1938 [ ] yes
OTC product [X] yes

6. If IND, protocol #

7. Type of report

- [ ] 5-day
- [ ] 15-day
- [ ] 10-day
- [X] periodic
- [ ] initial
- [X] follow-up # 1

8. Adverse event term(s)

Gastrointestinal haemorrhage
NOS

9. Mfr. report number

HQ1081615FEB2000

E. Initial reporter

1. Name & address

[redacted] phone # [redacted]

[redacted] Ave., Box # [redacted] Med. Ctr. School of Dentistry
US

JUL 17 2001

2. Health professional? [X] yes [ ] no

3. Occupation: Dentist/Oral Surgeon

4. Initial reporter also sent report to FDA: [ ] yes [ ] no [X] unk

FDA Form 3500A (facsimile)

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

WYETH AYERST

Individual Safety Report

3760817-3-00-02

MEDWATCH

IODUCTS REPORTING PROGRAM

Aporoved by the FDA on 09/24/1999

Mfr report #	HQ1081615FEB2000
UF/Dist report #	
	FDA Use Only

Box B.5 - Describe event or problem (Continuation)

the patient was admitted to the hospital and diagnosed with gastrointestinal hemorrhage (Gastrointestinal haemorrhage NOS). Event was determined to be severe (grade 3) according to the toxicity scale provided by the protocol. The patient was discharged from the hospital to resume normal activities. Information received 30-JUN-2000 indicated the patient had a mild chronic gastritis verified by an antral biopsy on 1-FEB-2000. The small bowel, colon, and terminal ileum were all normal. On 1-FEB-2000 the haemoglobin level was 12 g/dL and the haematocrit level was 36%. The medical monitor and the investigator considered the events not related to rhBMP-2/ACS implant. Both the medical monitor and the patient's private physician consider gastrointestinal hemorrhage possibly related to Advil. The investigator felt the event was related to the irritation of the gastrointestinal tract caused by the combination of medications the patient was taking.

Box B.6 - Relevant test/laboratory data, including dates (Continuation)

Test Name / *Date*	*Result*	*Normal Range*
Barium double contrast NOS		
02/09/2000	Normal colon and terminal ileum.	-
Biopsy NOS		
02/01/2000	Antral biopsy: mild chronic gastritis. No Helicobacter organisms identified on the "H&E" or special stained sections examined.	-
Haematocrit		
02/01/2000	36 %	37.0 - 49.0
Haemoglobin		
02/01/2000	12 g/dL	13.3 - 16.7
X-ray with contrast upper gastrointestinal tract		
02/11/2000	Small bowel series was normal.	-

Box C - Suspect medication(s) (Continuation from Lines #1 and #2 on original page)

1. Name (give labeled strength & mfr/labeler, if known)

2.1 (RHBMP-2) (RECOMBINANT HUMAN BONE MORPHOGENETIC PROTEIN-2 (RHBMP-2), Implant)

Box C.10 - Concomitant medical products and therapy dates (exclude treatment of event) (Continuation)

Therapy Name	*Dose, frequency, & route used*	*Therapy Dates*
CEPHALEXIN (CEFALEXIN)	500 mg 4x per 1 Day, Oral	01/11/2000 to 01/23/2000
PERIDEX (CHLORHEXIDINE GLUCONATE)	1 oz 2x per 1 Day, Oral	01/12/2000 to 01/21/2000
HYDROCODONE W/ACETAMINOPHEN (HYDROCODONE BITARTRATE/PARACETAMOL)	0.5 Tablet 2x per 1 Day, Oral	01/11/2000 to 01/12/2000
TETRACYCLINE (TETRACYCLINE)	500 mg 2x per 1 Day, Oral	10/23/1999 to 12/24/1999
TETRACYCLINE (TETRACYCLINE)	500 mg 3x per 1 Day, Oral	01/01/2000 to 01/02/2000
TETRACYCLINE (TETRACYCLINE)	500 mg 2x per 1 Day, Oral	01/03/2000 to 01/04/2000
NITROUS OXIDE (NITROUS OXIDE)	60%, Inhalation	01/11/2000 to 01/11/2000
MEPERIDINE HYDROCHLORIDE (PETHIDINE HYDROCHLORIDE)	50 mg 1x per 1 Day, Intravenous	01/11/2000 to 01/11/2000
METHOHEXITAL (METHOHEXITAL)	30 mg 1x per 1 Day, Intravenous	01/11/2000 to 01/11/2000
METHOHEXITAL (METHOHEXITAL)	10 mg 1x per 1 Day, Intravenous	01/11/2000 to 01/11/2000
DEXAMETHASONE (DEXAMETHASONE)	8 mg 1x per 1 Day, Intravenous	01/11/2000 to 01/11/2000
XYLOCAINE #1 (LIDOCAINE)	6 doses, Subcutaneous	01/11/2000 to 01/11/2000

JUL 17 2001

3774232-X-00-01

PHILADELPHIA, PA 19101

EDWATCH

PRODUCTS REPORTING PROGRAM

Approved by the FDA on 09/24/1999

Mfr report # HQ1183C22MAY2C01

UF/Dist report #

FDA Use Only

A. Patient information

1. Patient identifier	2. Age at time of event: or Date of Birth:	3. Sex	4. Weight
[redacted] in confidence	80Yr	[X] female [ ] male	84 lbs or kgs

B. Adverse event or product problem

1. [X] Adverse event [ ] Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)

- [ ] death (mo/day/yr)
- [ ] life-threatening
- [X] hospitalization-initial or prolonged
- [ ] recovered
- [ ] disability
- [ ] congenital anomaly
- [ ] required intervention to prevent permanent impairment/damage
- [ ] other:

3. Date of event (mo/day/yr)	4. Date of this report (mo/day/yr)
12/21/1999	08/08/2001

5. Describe event or problem

Upon subsequent review the following fields have been modified: event details and narrative. Follow up information was received on 25-JUN-2001 from a healthcare professional updating the patient's course. Initial information was received on 21-MAY-2001 from an 80-year old female patient. The patient's concurrent illnesses anemia since 1998, and hypertension with a past history of toe surgery subsequent to a foot fracture. Therapy with Advil (ibuprofen)(tablet) for arthritis NOS began on 21-NOV-1999 and ended on 28-APR-2001(drug maladministration). The dose regimen was one tablet by mouth once daily. Concomitant therapy included Vitamin e (tocopherol),Centrum (multivitamin/multimineral), and Monopril (fosinopril sodium). The patient was admitted to the hospital after experiencing "melenic stools" (melaena) followed by episodes of hematemesis (haematemesis) and subsequent light headedness (dizziness exc vertigo). The patient also complained of weakness (weakness), fatigue

(cont'd)

6. Relevant tests/laboratory data, including dates

See following page.

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

CONCURRENT CONDITIONS:
Anaemia NOS; Hypertension NOS

PAST CONDITIONS:
Operation NOS; Foot fracture

AUG 08 2001
DATE SENT TO FDA

C. Suspect medication(s)

RECEIVED
AUG 09 2001
CDR/CDER

1. Name (give labeled strength & mfr/labeler, if known)

#1 ADVIL (IBUPROFEN) Tablet 200 mg)

#2

2. Dose, frequency & route used	3. Therapy dates (if unknown, give duration)
#1 1 Tablet 1x per 1 Day, Oral	#1 11/21/1999 to 04/28/2001
#2	#2

4. Diagnosis for use (indication)	5. Event abated after use stopped or dose reduced
#1 Arthritis NOS	#1 [ ] yes [ ] no [X] doesn't apply
#2	#2 [ ] yes [ ] no [ ] doesn't apply

6. Lot # (if known)	7. Exp date (if known)	8. Event reappeared after reintroduction
#1	#1	#1 [ ] yes [ ] no [X] doesn't apply
#2	#2	#2 [ ] yes [ ] no [ ] doesn't apply

9. NDC # - for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)

See following Page.

G. All manufacturers

1. Contact office - name/address

WHITEHALL-ROBINS
201 King of Prussia
Sixth Floor
Radnor, PA 19087-5114

Jill Robinson

2. Phone number: 6109644680

3. Report source. (check all that apply)

- [ ] foreign
- [ ] study
- [ ] literature
- [ ] consumer
- [X] health professional
- [ ] user facility
- [ ] company representative
- [ ] distributor
- [ ] other:

4. Date received by manufacturer (mo/day/yr): 08/02/2001

5. (A)NDA 1) 18-989
IND #
PLA #
pre-1938 [ ] yes
OTC product [X] yes

6. If IND, protocol #

7. Type of report

- [ ] 5-day [X] 15-day
- [ ] 10-day [ ] periodic
- [ ] initial [X] follow-up # 2

8. Adverse event term(s)

Gastric ulcer
Fatigue
Drug maladministration
Haematemesis
Melaena
Weakness
Dizziness (exc vertigo)
(cont'd)

DSS
AUG 10 2001

9. Mfr. report number: HQ1183022MAY2001

E. Initial reporter

1. Name & address: [redacted], Dr. [redacted] US

phone # [redacted]

AUG 09 2001

2. Health professional?	3. Occupation	4. Initial reporter also sent report to FDA
[X] yes [ ] no	Physician	[ ] yes [ ] no [X] unk

FDA Form 3500A (facsimile)

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

WYETH

3774232-X-00-02

MEDWATCH

L PRODUCTS REPORTING PROGRAM

Approved by the FDA on 09/24/1999

Mfr report #	HQ1183022MAY2001
UF/Dist report #	
	FDA Use Only

Box B.5 - Describe event or problem (Continuation)

(fatigue), and lightheadedness over the day or two proceeding the hospital admission. On admission, the patient was found to be anemic (anaemia NOS) with normocytic indices. The patient's subsequent esophagogastroduodenoscopy revealed a 1 cm ulcer in the lesser curvature of the stomach body (gastric ulcer) , as well as erosive gastritis (gastric erosions) and mild duodenitis (duodenitis) within the stomach bulb. The patient, who experienced no weight loss according to the physician, was found to have prerenal azotemia (acute pre-renal failure). The physician attributed the elevation in blood urea nitrogen secondary to the gastrointestinal bleed. The patient's laboratory tests consisted of the following; a white blood cell count of 7900 cells, hemoglobin of 6.1g/dL, hematocrit of 18.6%, platelets of 257,000, an Mean cell volume of 96 fl, a Red blood cell distribution width of 14.3, a BUN of 79 g/day, a blood creatinine of 1.2 g/dL, an International normalized ratio of 1.2, a prothrombin time of 26 seconds, a body temperature of 99.7 deg.F, a heart rate of 82 beats per minute, and respiratory rate of 20 breaths per minute, a blood pressure of 141/50 mmHg, and a weight loss from 110 pounds to 84 pounds according to the patient. The patient's adverse event improved when the drug was discontinued. Also, the patient has not recovered from her symptoms.

Box B.6 - Relevant test/laboratory data, including dates (Continuation)

Test Name / *Date*	*Result*	*Normal Range*
Biopsy bone marrow	"ruled out malignancy"	-
Blood creatinine	1.2 g/dL	-
Blood pressure	141/.50 mmHg	-
Blood urea	79 g/d	-
Body temperature	99.7 deg. F.	-
Endoscopy NOS	revealed 1 cm ulcer in the lesser curvature of the body of the stomach. There was a visible vessel in the nearby mucosa. There was also erosive gastritis and mild duodenitis	-
Haematocrit	"found to be anemic with normocytic indices"	-
	18.6 %	-
Haemoglobin	6.1 g/dL	-
Heart rate	"82 "	-
International normalised ratio	1.2	-
Mean cell volume	"96"	-
Platelet count	257,000 cells	-
Prothrombin time	26 seconds	-
Respiratory rate	"20"	-
Weight	lost weight (from 110 pounds to 84 pounds)	-
White blood cell count	7900 cells/uL	-

DSS

AUG 1 0 2001

AUG 0 9 2001

Approved by the FDA on 09/24/1999

Mfr report #	HQ1183022MAY2001
UF/Dist report #	
	FDA Use Only

Box C.10 - Concomitant medical products and therapy dates (exclude treatment of event) (Continuation)

Therapy Name	*Dose, frequency, & route used*	*Therapy Dates*
VITAMIN E (TOCOPHEROL)	400 IU 1x per 1 Day, Oral	12/00/2000 to Continues
CENTRUM (MULTIVITAMIN/MULTIMINERAL)	1 Tablet 1x per 1 Day, Oral	00/00/1999 to Continues
MONOPRIL (FOSINOPRIL SODIUM)	unknown, Oral	unknown

Box G.8 - Adverse event term(s) (Continuation)

Acute pre-renal failure
Anaemia NOS
Gastric erosions
Duodenitis

DSS

AUG 1 0 2001

AUG 0 9 2001

Individual Safety Report

3777317-7-00-01

...LUNTARY reporting
...h professionals of adverse
...s and product problems

Page of (CDER)

Form Approved: OMB No. 0910-0291 Expires: 12/31/94
See OMB statement on reverse

FDA Use Only

Triage unit sequence # 148920

A. Patient information

1. Patient identifier: 01-43 (In confidence)
2. Age at time of event: or Date of birth: [redacted]
3. Sex: [X] female [ ] male
4. Weight: 153 lbs or ____ kgs

B. Adverse event or product problem

1. [X] Adverse event and/or [ ] Product problem (e.g., defects/malfunctions)
2. Outcomes attributed to adverse event (check all that apply)
   - [ ] death (mo day yr)
   - [ ] life-threatening
   - [X] hospitalization – initial or prolonged
   - [ ] disability
   - [ ] congenital anomaly
   - [ ] required intervention to prevent permanent impairment/damage
   - [ ] other:
3. Date of event (mo day yr): 4/25/2001
4. Date of this report (mo day yr): 8/8/2001
5. Describe event or problem

The patient was admitted to the hospital because of a duodenal ulcer secondary to non-steroidal anti-inflammatory drugs. The pt. had a rebleed 4 days after and required a repeat endoscopy. The pt. did stop bleeding
Pt. was put on Prevacid 30mg PO BID.
Upon ER admission, pt. had black/maroon colored stools.

6. Relevant tests/laboratory data, including dates

4/25/01 : RBC = 3.77, HGB = 10.1, HCT = 30.5
5/10/01 : RBC = 4.05, HGB = 11.5, HCT = 33.9

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

Advanced non-Small cell lung CA
Pt. on radiation & chemo
Stage I Breast CA
Thyroid Goiter
CTV148920

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
   #1 Advil
   #2
2. Dose, frequency & route used
   #1 12 tabs/day PO
   #2
3. Therapy dates (if unknown, give duration) (from to or best estimate)
   #1 PTA
   #2
4. Diagnosis for use (indication)
   #1 Pain
   #2
5. Event abated after use stopped or dose reduced
   #1 [X] yes [ ] no [ ] doesn't apply
   #2 [ ] yes [ ] no [ ] doesn't apply
6. Lot # (if known)
   #1 unknown
   #2
7. Exp. date (if known)
   #1 unknown
   #2
8. Event reappeared after reintroduction
   #1 [ ] yes [ ] no [X] doesn't apply
   #2 [ ] yes [ ] no [ ] doesn't apply
9. NDC # (for product problems only)
   - -
10. Concomitant medical products and therapy dates (exclude treatment of event)
    Taxol, Tamoxifen

D. Suspect medical device

1. Brand name
2. Type of device
3. Manufacturer name & address

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4. Operator of device
   - [ ] health professional
   - [ ] lay user/patient
   - [ ] other:
5. Expiration date (mo day yr)
6. model #
   catalog #
   serial #
   lot #
   other #
7. If implanted, give date (mo day yr)
8. If explanted, give date (mo day yr)
9. Device available for evaluation? (Do not send to FDA)
   [ ] yes [ ] no [ ] returned to manufacturer on (mo day yr)

DSS
AUG 15 2001

10. Concomitant medical products and therapy dates (exclude treatment of event)

E. Reporter (see confidentiality section on back)

1. Name, address & phone #
   [redacted] Hospital Ave.
2. Health professional? [X] yes [ ] no
3. Occupation: Pharmacist
4. As reported to
   - [ ] manufacturer
   - [ ] user facility
   - [ ] distributor
5. If you do NOT want your identity disclosed to the manufacturer, place an "X" in this box. [X]

FDA

Mail to: MEDWATCH, 5600 Fishers Lane, Rockville, MD 20852-9787
or FAX to: 1-800-FDA-0178

FDA Form 3500 (6/93)

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

Individual Safety Report

3778270-2-00-01

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

VOLUNTARY reporting ...ealth professionals of adverse ...vents and product problems

Page ... of ... (D&K

Form Approved: OMB No. 0910-0291 Expires: 12/31/94
See OMB statement on reverse

FDA Use Only

Triage unit sequence # 149152

DEXIN-FAX

A. Patient information

1. Patient identifier: 117-693 (in confidence)
2. Age at time of event: 94 or ... Date of birth:
3. Sex: ☐ female ☐ male
4. Weight: ... lbs or ... kgs

B. Adverse event or product problem

1. ☒ Adverse event and/or ☐ Product problem (e.g., defects/malfunctions)
2. Outcomes attributed to adverse event (check all that apply)
   - ☒ death ... (mo/day/yr)
   - ☐ life-threatening
   - ☐ hospitalization - initial or prolonged
   - ☐ disability
   - ☐ congenital anomaly
   - ☐ required intervention to prevent permanent impairment/damage
   - ☐ other: ...
3. Date of event (mo/day/yr): 05-00
4. Date of this report (mo/day/yr): 06-07-01
5. Describe event or problem:

Death due to complication from GI Bleed & Severe (OP)

6. Relevant tests/laboratory data, including dates

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

CTV149152

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
   #1 Advil
2. Dose, frequency & route used
   #1
   #2
3. Therapy dates (if unknown, give duration) (mo/day/yr)
   #1
   #2
4. Diagnosis for use (indication)
   #1
   #2
5. Event abated after use stopped or dose reduced
   #1 ☐ yes ☐ no ☐ doesn't apply
   #2 ☐ yes ☐ no ☐ doesn't apply
6. Lot # (if known)
   #1
7. Exp. date (if known)
   #1
8. Event reappeared after reintroduction
   #1 ☐ yes ☐ no ☐ doesn't apply
   #2 ☐ yes ☐ no ☐ doesn't apply
9. NDC # (for product problems only)
   - -
10. Concomitant medical products and therapy dates (exclude treatment of event)

D. Suspect medical device

1. Brand name
2. Type of device
3. Manufacturer name & address

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6 model # MEDWATCH CTU
catalog #
serial #
lot #
other #

4. Operator of device
   - ☐ health professional
   - ☐ lay user/patient
   - ☐ other
5. Expiration date (mo/day/yr)
7. If implanted, give date (mo/day/yr)
8. If explanted, give date (mo/day/yr)
9. Device available for evaluation? (Do not send to FDA)
   ☐ yes ☐ no ☐ returned to manufacturer on ... (mo/day/yr)

DSS
AUG 16 2001

10. Concomitant medical products and therapy dates (exclude treatment of event)

E. Reporter (see confidentiality section on back)

1. [redacted] Ph.D., FASCP, R.Ph.
   Director of Pharmacy Services
   [redacted] Avenue
   P.O. Box [redacted]
   Memorial Hospital
2. Health professional? ☒ yes ☐ no
3. Occupation: Pharmacist
4. Also reported to
   - ☒ manufacturer
   - ☐ user facility
   - ☐ distributor
5. If you do NOT want your identity disclosed to the manufacturer, place an " X " in this box. ☐

FDA

Mail to: MEDWATCH, 5600 Fishers Lane, Rockville, MD 20852-9787
or FAX to: 1-800-FDA-0178

FDA Form 3500 (6/93)

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

Individual Safety Report

3778431-2-00-01

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

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:s and product problems

Page ___ of ___ CONT

Form Approved: OMB No. 0910-0291 Expires: 12/31/94
See OMB statement on reverse

FDA Use Only

Triage unit sequence # 149140

A. Patient information

1. Patient identifier: 38-371 In confidence
2. Age at time of event: 52 or Date of birth:
3. Sex: ☐ female ☐ male
4. Weight: ___ lbs or ___ kgs

B. Adverse event or product problem

1. ☒ Adverse event and/or ☐ Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)
- ☐ death (mo/day/yr)
- ☐ life-threatening
- ☐ hospitalization – initial or prolonged
- ☐ disability
- ☐ congenital anomaly
- ☐ required intervention to prevent permanent impairment/damage
- ☒ other: Resolved

3. Date of event (mo/day/yr): 07-00
4. Date of this report (mo/day/yr): 06-07-01

5. Describe event or problem
melanotic stools

6. Relevant tests/laboratory data, including dates

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

CTV149140

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
#1 Aspirin 4A-Ltd

2. Dose, frequency & route used
#1
#2

3. Therapy dates (if unknown, give duration) (mo/day/yr or best estimate)
#1
#2

4. Diagnosis for use (indication)
#1
#2

5. Event abated after use stopped or dose reduced
#1 ☐ yes ☐ no ☐ doesn't apply
#2 ☐ yes ☐ no ☐ doesn't apply

6. Lot # (if known)
#1

7. Exp. date (if known)
#1

8. Event reappeared after reintroduction
#1 ☐ yes ☐ no ☐ doesn't apply
#2 ☐ yes ☐ no ☐ doesn't apply

9. NDC # (for product problems only)
- -

10. Concomitant medical products and therapy dates (exclude treatment of event)

D. Suspect medical device

1. Brand name

2. Type of device

3. Manufacturer name & address

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MEDWATCH CTU

4. Operator of device
- ☐ health professional
- ☐ lay user/patient
- ☐ other:

5. Expiration date (mo/day/yr)

6. model #
catalog #
serial #
lot #
other #

7. If implanted, give date (mo/day/yr)

8. If explanted, give date (mo/day/yr)

9. Device available for evaluation? (Do not send to FDA)
☐ yes ☐ no ☐ returned to manufacturer on (mo/day/yr)

10. Concomitant medical products and therapy dates (exclude treatment of event)

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AUG 16 2001

E. Reporter (see confidentiality section on back)

1. [redacted]
Ph.D., FASCP, R.Ph.
Director of Pharmacy Services
[redacted] Avenue
P.O. Box [redacted]
Memorial Hospital

2. Health professional? ☒ yes ☐ no

3. Occupation: Pharmacist

4. Also reported to
- ☒ manufacturer
- ☐ user facility
- ☐ distributor

5. If you do NOT want your identity disclosed to the manufacturer, place an " X " in this box. ☐

FDA

Mail to: MEDWATCH, 5600 Fishers Lane, Rockville, MD 20852-9787
or FAX to: 1-800-FDA-0178

FDA Form 3500 (6/93)

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

Individual Safety Report

3803406-4-00-01

For VOLUNTARY reporting
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Page ___ of ___

See OMB statement on rev

FDA Use Only

Triage unit sequence # 152872

A. Patient information

1. Patient identifier	2. Age at time of event: / or Date of birth:	3. Sex	4. Weight
[redacted]1537 In confidence	52 / [redacted]	☐ female ☒ male	___ lbs or ___ kgs

B. Adverse event or product problem

1. ☒ Adverse event and/or ☐ Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)

- ☐ death ___ (mo/day/yr)
- ☐ life-threatening
- ☒ hospitalization – initial or prolonged
- ☐ disability
- ☐ congenital anomaly
- ☐ required intervention to prevent permanent impairment/damage
- ☐ other: ___

3. Date of event (mo/day/yr)	4. Date of this report (mo/day/yr)
7/31/01	8/01

5. Describe event or problem

H/O 2 DAYS NV, epigastric pain (hematemesis)

TX c Sandostatin 50mcg bolus, followed by 50c/hr. Ranitidine 50mg IV q8h Lansoprazole. FFP Jumbo.

6. Relevant tests/laboratory data, including dates

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

EtOH use

H. pylori +

CTV152872

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)

#1 VIOXX

#2 Ibuprofen (OTC) and Aspirin

2. Dose, frequency & route used	3. Therapy dates (if unknown, give duration) (from/to (or best estimate))
#1 25mg qd	#1 4 DAYS?
#2 600mg qd?	#2

4. Diagnosis for use (indication)	5. Event abated after use stopped or dose reduced
#1 GSB 4 HR	#1 ☐ yes ☐ no ☐ doesn't apply
#2 OSTEOARTHRITIS PAIN	#2 ☐ yes ☐ no ☐ doesn't apply

6. Lot # (if known)	7. Exp. date (if known)	8. Event reappeared after reintroduction
#1	#1	#1 ☐ yes ☐ no ☐ doesn't apply
#2	#2	#2 ☐ yes ☐ no ☐ doesn't apply

9. NDC # (for product problems only) – –

10. Concomitant medical products and therapy dates (exclude treatment of event)

D. Suspect medical device

1. Brand name

2. Type of device

3. Manufacturer name & address

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MEDWATCH CTU

4. Operator of device
- ☐ health professional
- ☐ lay user/patient
- ☐ other: ___

5. Expiration date (mo/day/yr)

6. model # ___
catalog # ___
serial # ___
lot # ___
other # ___

7. If implanted, give date (mo/day/yr)

8. If explanted, give date (mo/day/yr)

9. Device available for evaluation? (Do not send to FDA)
☐ yes ☐ no ☐ returned to manufacturer on ___ (mo/day/yr)

10. Concomitant medical products and therapy dates (exclude treatment of event)

OCT 0

E. Reporter (see confidentiality section on back)

1. Name, address & phone #

[redacted]

2. Health professional?	3. Occupation	4. Also reported to
☒ yes ☐ no	PCP	☐ manufacturer

Submission of a report does not constitute an admission that medical personnel or the product

Individual Safety Report

3823641-9-00-01

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

For use by user-facilities, distributors and manufacturers for MANDATORY reporting
Pharmacia & Upjohn, Inc.

Fielsys International, Inc.
FDA Facsimile Approval: 30-JUN-1999

Mfr report #: 2001078518US
IND/Dist report #:

FDA Use Only

A. Patient information

1. Patient identifier	2. Age at time of event: / or Date of birth:	3. Sex	4. Weight
UNK in confidence	52 years / UNK	[ ] female [X] male	UNK lbs or UNK kgs

B. Adverse event or product problem

1. [X] Adverse event and/or [ ] Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)
- [ ] death (mo/day/yr)
- [ ] life-threatening
- [ ] hospitalization - initial or prolonged
- [ ] disability
- [ ] congenital anomaly
- [ ] required intervention to prevent permanent impairment/damage
- [X] other: Medically Significant

3. Date of event (mo/day/yr): UNK

4. Date of this report (mo/day/yr): 11/07/2001

5. Describe event or problem

Anemia[Anaemia NOS]
Melaena[Melaena]
Small bowel diaphragms and strictures[Small intestinal obstruction NOS]

Case Description:
Spontaneous literature

A 52-year-old male patient received ibuprofen (600 mg/daily) for at least 15 years to control pain associated with osteoarthritis. He developed melaena, recurrent obscure gastrointestinal bleeding and iron-deficiency anemia. His hemoglobin declined to 1.5 mmol/L. Intraoperative enteroscopy to the terminal ileum was performed, which showed three distinct diaphragm-like strictures in a 34 cm long area of the dismal ileum. Ibuprofen treatment was discontinued after the first episode of melaena. The patient denied any current use
continued in additional info section...

6. Relevant tests/laboratory data, including dates

Hemoglobin: 1.5 mmol/L
Intraoperative enteroscopy to the terminal ileum: three distinct diaphragm-like strictures in a 34 cm long area of the distal ileum

7. Other relevant history, including preexisting medical conditions (e.g. allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

NI

NOV 1 2 2001

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)

1. NUPRIN(IBUPROFEN) (continued).
2.

2. Dose, frequency & route used	3. Therapy dates (if unknown, give duration) (from/to (or best estimate))
# 1. 600 mg, qd, UNK	# 1. UNK
# 2.	# 2.

4. Diagnosis for use (indication)
1. Pain NOS
2.

5. Event abated after use stopped or dose reduced
1. [ ] yes [ ] no [ ] doesn't apply UNK
2. [ ] yes [ ] no [ ] doesn't apply

6. Lot # (if known)
1. UNK
2.

7. Exp. date (if known)
1. UNK
2.

8. Event reappeared after reintroduction
1. [ ] yes [ ] no [ ] doesn't apply UNK
2. [ ] yes [ ] no [ ] doesn't apply

9. NDC # - for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)

NI

G. All Manufacturers

1. Contact office - name/address (& mfring site for devices)
Pharmacia
Donald M. Demke, M.D.
Safety Officer
7031-248-USPV
7000 Portage Road
Kalamazoo, MI 49001 UNITED STATES

2. Phone number: (616)833-8777

3. Report source (check all that apply)
- [ ] foreign
- [ ] study
- [ ] literature
- [ ] consumer
- [X] health professional
- [ ] user facility
- [ ] company representative
- [ ] distributor
- [ ] other:

4. Date received by manufacturer (mo/day/yr): 10/29/2001

5. (A)NDA # 19012
IND #
PLA #
pre-1938 [ ] yes
OTC product [ ] yes

6. If IND, protocol #

7. Type of report (check all that apply)
- [ ] 5-day [X] 15-day
- [ ] 10-day [ ] periodic
- [X] initial [ ] follow-up #

8. Adverse event term(s)
Anaemia NOS, Melaena, Small intestinal obstruction NOS

9. Mfr. report number
2001078518US

E. Initial reporter

1. Name & address
[redacted]
[redacted] University
[redacted] UNITED STATES

phone # UNK

DSS

NOV 1 3 2001

2. Health professional ?	3. Occupation	4. Initial report also sent report to FDA?
[X] yes [ ] no	other health professional	[ ] yes [ ] no [X] unk

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

FDA

3500A - Facsimile

Additional Information

B5. EVENT DESCRIPTION (cont.)

of NSAID.
The events are considered serious as medically significant. After 6 months the patient presented for a follow up and no further bleeding had occurred.

Case Comment:
The reported event bowel obstruction in not listed in the Core Data Sheet of ibuprofen. The physiopathological link between the ibuprofen administration and the reported bowel obstruction is not obvious. A subcronic phlogistic injury by ibuprofen can be suspected but an evidence-based documentation seems difficult to be obtained.

Submission of a report does not constitute an admission that the medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

C1. Name (cont.)
Suspect Medication #1: NUPRIN(IBUPROFEN) tablet

MEDWATCH
THE
Comp

3825072-4-00-01

Form Approved by FDA 05/13/97

For MANDATORY reporting.

Mfr. report # 01-126

UF/Dist.report #

FDA Use Only

Page 1 of 11

A. Patient information

1. Patient identifier	2. Age at time of event:	3. Sex	4. Weight
Unk in confidence	or 12 Date of birth: Unk	☒ female ☐ male	Unk lbs or _____ kgs

B. Adverse event

1. ☒ Adverse event and/or ☐ Product problem (eg, defect/malfunct.)

2. Outcomes attributed to adverse event (check all that apply)
- ☐ death _____
- ☐ life-threatening
- ☒ hospitalization-initial or prolonged
- ☐ disability
- ☐ congenital anomaly
- ☐ required intervention to prevent permanent impairment/damage
- ☐ other: _____

3. Date of event	4. Date of report
(mo/day/yr) 09/20/96-02/97	(mo/day/yr) 10/31/01

5. Describe event

High-dose Ibuprofen therapy for cystic fibrosis was associated with the development of pyloric channel stricture in a 12-year girl. Approximately 2 months after starting Ibuprofen 1000 mg (28.2 mg/kg/dose) given twice daily, the girl began to experience episodes of emesis and was unable to tolerate solid foods. She began treatment with cisapride and ranitidine, but her emesis and food tolerance persisted over the next 3 months and she lost 7 kg in body weight. Un upper endoscopy performed approximately 5 months after the start of Ibuprofen therapy revealed pyloric channel stenosis and obstruction. Pyloric channel dilation was successfully performed. Ibuprofen and ranitidine were discontinued and the girl began treatment with omeprazole. At follow-up approximately 6 months later the girl was not experiencing any emesis or dysphagia and had gained 8.1 kg in body weight.

[1] Bell, ES, Grothe R, Zivkovich V et al., "Pyloric Channel Stricture Secondary to High Dose Ibuprofen Therapy in a Patient with Cystic Fibrosis", Ann Pharmacother 1999; 33; 693-696.

6. Relevant tests/laboratory data, including dates
Unk

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking, and alcohol use, hepatic/renal dysfunction, etc.)
Cystic Fibrosis

C. Suspect medication(s)

1. Name (give labeled strength & mfr./labeler, if known)
1 Ibuprofen , Unk, Unk

2

2. Dose, frequency & route used	3. Therapy dates
# 1 2000 mg/day/oral	# 1 09/20/96 - 02/97
# 2	# 2

4. Diagnosis for use (indication)	5. Event abated after use stopped or dose reduced
# 1 pulmonary manifestations of CF	# 1 ☒ yes ☐ no ☐ n/a
# 2	# 2 ☐ yes ☐ no ☐ n/a

6. Lot #	7. Exp. date	8. Event reappeared after reintroduction
# 1 Unk	# 1 Unk	# 1 ☐ yes ☐ no ☒ n/a
# 2	# 2	# 2 ☐ yes ☐ no ☐ n/a

9. NDC # - for product problems only (if known)
- -

10. Concomitant medical products and therapy dates (exclude treatment of event)
Pancrelipase, dornase alfa, 2.5 mg.

D. All manufacturers

1. Contact office - name & address
Par Pharmaceutical, Inc.
One Ram Ridge Road
Spring Valley, New York 10977

2. Phone number
914-425-7100

3. Report source(s)
- ☐ foreign
- ☐ study
- ☒ literature
- ☐ consumer
- ☒ health professional
- ☐ user facility
- ☐ company representative
- ☐ distributor
- ☐ other: _____

4. Date received by manufacturer
07/09/01

5. ANDA # Unk
IND # _____
PLA # _____
pre-1938 ☐ yes
OTC Product ☐ yes

6. If IND, protocol #
N/A

7. Type of report
- ☐ 5-day ☒ initial
- ☐ 10-day ☐ 15-day
- ☒ periodic
- ☐ follow-up # _____

8. Adverse event term(s)
Pyloric channel stricture

9. Mfr. report #
01-126

E. Initial reporter

1. Name, address & phone number
Bayer AG
Global Product Safety (GDS)
Morristown, NJ 07962-1910 (973) 254-5000

2. Health professional?	3. Occupation	4. Initial reporter also sent report to FDA
☒ yes ☐ no	Pharm. Co.	☐ yes ☐ no ☒ unk

NOV 14 2001

FDA Form 3500A Facsimile

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

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Form Approved by FDA 05/13/97

For **MANDATORY** reporting.

Page 2 of 11

Mfr. report # 01-127
UF/Dist.report #
FDA Use Only

A. Patient information

1. Patient identifier	2. Age at time of event:	3. Sex	4. Weight
Unk in confidence	or 18 months Date of birth: Unk	☐ female ☒ male	___ lbs or 12 kgs

B. Adverse event

1. ☒ Adverse event and/or ☐ Product problem (eg, defect/malfunct.)

2. Outcomes attributed to adverse event (check all that apply)
- ☐ death _____
- ☐ life-threatening
- ☒ hospitalization-initial or prolonged
- ☐ disability
- ☐ congenital anomaly
- ☐ required intervention to prevent permanent impairment/damage
- ☐ other: _____

3. Date of event (mo/day/yr)	4. Date of report (mo/day/yr)
Unk	10/31/01

5. Describe event

This case involves an 18 month-old male child who took Ibuprofen and developed emesis, apnia, lethargy and tonic clonic seizures. The patient, with an unremarkable past was brought to the Emergency Room by the parents 4hours prior to presentation with an empty bottle of Ibuprofen and with tablet fragments in his mouth. He had 2 episodes of emesis. After a brief period of relatively normal behavior, the parents noticed the patient became limp and was not easily aroused. The patient subsequently became apneic, prompting the parents to bring him to the ER. Investigation indicated a potential ingestion of as much as 7.2 g of Ibuprofen (600 mg/kg). Activated charcoal was then administered. A sodium bicarbonate bolus of 12 mEq was administered, followed by an infusion of DSW and 24 mEq/L sodium bicarbonate at 90 mL per hour in light of the patient's acidosis. The patient was discharged two days later with an uneventful recovery.

[1] E. E. Oker, L. Herman, C. R. Baum, K. M. Fentzke, T. Sigg, J. B. Leiken, "Serious Toxicity in a Young Child due to Ibuprofen", (Academic Emergency Medicine) 7/2000, Vol. 7, No. 7, P. 821-823.

6. Relevant tests/laboratory data, including dates
Unk

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking, and alcohol use, hepatic/renal dysfunction, etc.)
Unknown

C. Suspect medication(s)

1. Name (give labeled strength & mfr./labeler, if known)
1 Ibuprofen , unk, unk

2

2. Dose, frequency & route used	3. Therapy dates
# 1 Accidental Overdose/Infant	# 1 Unk
# 2	# 2

4. Diagnosis for use (indication)	5. Event abated after use stopped or dose reduced
# 1	# 1 ☒ yes ☐ no ☐ n/a
# 2	# 2 ☐ yes ☐ no ☐ n/a

6. Lot #	7. Exp. date	8. Event reappeared after reintroduction
# 1 Unk	# 1 Unk	# 1 ☐ yes ☐ no ☒ n/a
# 2	# 2	# 2 ☐ yes ☐ no ☐ n/a

9. NDC # - for product problems only (if known)
- -

10. Concomitant medical products and therapy dates (exclude treatment of event)
Pseudoephedrine

D. All manufacturers

1. Contact office - name & address

Par Pharmaceutical, Inc.
One Ram Ridge Road
Spring Valley, New York 10977

2. Phone number
914-425-7100

4. Date received by manufacturer	5.
02/02/01	ANDA # UNK IND # _____ PLA # _____ pre-1938 ☐ yes OTC Product ☐ yes
6. If IND, protocol # N/A	
7. Type of report ☐ 5-day ☒ initial ☐ 10-day ☐ 15-day ☒ periodic ☐ follow-up # _____	

3. Report source(s)
- ☐ foreign
- ☐ study
- ☒ literature
- ☐ consumer
- ☒ health professional
- ☐ user facility
- ☐ company representative
- ☐ distributor
- ☐ other: _____

8. Adverse event term(s)	9. Mfr. report #
Lethargy, apnea, Tonic Clonic Seizure, emesis	01-127

E. Initial reporter

1. Name, address & phone number
Bayer AG
Global Product Safety (GDS)
Morristown, NJ 07962-1910 (973) 254-5000

2. Health professional?	3. Occupation	4.Initial reporter also sent report to FDA
☒ yes ☐ no	Pharm. Co.	☐ yes ☐ no ☒ unk

NOV 14 2001

FDA Form 3500A Facsimile

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

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3825072-4-00-03

Form Approved by FDA 05/13/97

For **MANDATORY** reporting.

Mfr. report # 01-135

UF/Dist.report #

FDA Use Only

A. Patient information

1. Patient identifier	2. Age at time of event:	3. Sex	4. Weight
Unk in confidence	or 55 Date of birth:	☐ female ☒ male	Unk lbs or _____ kgs

B. Adverse event

1. ☒ Adverse event and/or ☐ Product problem (eg, defect/malfunct.)

2. Outcomes attributed to adverse event (check all that apply)
- ☐ death _____
- ☐ life-threatening
- ☒ hospitalization-initial or prolonged
- ☐ disability
- ☐ congenital anomaly
- ☐ required intervention to prevent permanent impairment/damage
- ☐ other: _____

3. Date of event (mo/day/yr)	4. Date of report (mo/day/yr)
Unk	10/31/01

5. Describe event

A 55-year old male patient was presented to a hospital for surgical treatment of avascular necrosis of both hips. He had been using Nonsteroidal antiinflammatory drugs and steroids, (piroxicam, ibuprofen and betamethassone) for 4 years to relieve hip joint pain. In addition he began to complain of epigastric pain with a duration of 1 month. Therefore and endoscopy was performed 1 month before hospital admission, revealing an active ulceration in the prepyloric antrum. At that time, there was no evidence of duodenal obstruction. At admission the patient complained of frequent vomiting. Upper G.I. series revealed smooth narrowing of the pyloric channel and marked distension of the first and second portion of the duodenum. Exploratory laparotomy was performed. Duodenotomy revealed an incomplete 3-mm-thick diaphragm at the third portion of the duodenum. During surgery, total excision of the diaphragm and subtotal gastrectomy were performed. The patient was discharged from the hospital and had an uneventful recovery with complete relief of obstructive symptoms.

[1] Sung Eun Rha, Jae Hee Lee, Sung Yong Lee, Soung Man Park, "Duodenal Diaphragm Associated with Long-Term Use of Nonsteroidal Antiinflammatory Drugs: A Rare Cause of Duodenal Obstruction in an Adult", AJR 2000; 175:920-921.

6. Relevant tests/laboratory data, including dates

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking, and alcohol use, hepatic/renal dysfunction, etc.)

Avascular necrosis of both hips

C. Suspect medication(s)

1. Name (give labeled strength & mfr./labeler, if known)

1 Ibuprofen Tablets, Unk, Unk

2

2. Dose, frequency & route used	3. Therapy dates
# 1 Unk	# 1
# 2	# 2

4. Diagnosis for use (indication)	5. Event abated after use stopped or dose reduced
# 1 Hip Joint pain	# 1 ☐ yes ☐ no ☒ n/a
# 2	# 2 ☐ yes ☐ no ☐ n/a

6. Lot #	7. Exp. date	8. Event reappeared after reintroduction
# 1 Unk	# 1 Unk	# 1 ☐ yes ☐ no ☒ n/a
# 2	# 2	# 2 ☐ yes ☐ no ☐ n/a

9. NDC # - for product problems only (if known)

- -

10. Concomitant medical products and therapy dates (exclude treatment of event)

D. All manufacturers

1. Contact office - name & address

Par Pharmaceutical, Inc.
One Ram Ridge Road
Spring Valley, New York 10977

2. Phone number 914-425-7100

3. Report source(s)
- ☒ foreign
- ☐ study
- ☒ literature
- ☐ consumer
- ☒ health professional
- ☐ user facility
- ☐ company representative
- ☐ distributor
- ☐ other: _____

4. Date received by manufacturer	5.
02/02/01	ANDA # UNK IND # _____ PLA # _____ pre-1938 ☐ yes OTC Product ☐ yes
6. If IND, protocol #	
N/A	
7. Type of report	
☐ 5-day ☒ initial	
☐ 10-day ☐ 15-day	
☒ periodic	
☐ follow-up # _____	

8. Adverse event term(s)

Prepyloric ulcer, epigastric pain, duodenal diaphragm, vomiting

9. Mfr. report # 01-135

E. Initial reporter

1. Name, address & phone number

Bayer AG
Global Product Safety (GDS)
Morristown, NJ 07962-1910 (973) 254-5000

2. Health professional?	3. Occupation	4.Initial reporter also sent report to FDA
☒ yes ☐ no	Pharm. Co.	☐ yes ☐ no ☒ unk

FDA Form 3500A Facsimile

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

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Individual Safety Report
3825072-4-00-04

For **MANDATORY** reporting.

Page 4 of 11

Form Approved by FDA 05/13/97

Mfr. report # 01-136
UF/Dist.report #
FDA Use Only

A. Patient information

1. Patient identifier	2. Age at time of event: or Date of birth:	3. Sex	4. Weight
in confidence		☐ female ☒ male	Unk lbs or ____ kgs

B. Adverse event

1. ☒ Adverse event and/or ☐ Product problem (eg, defect/malfunct.)

2. Outcomes attributed to adverse event (check all that apply)
- ☐ death ____
- ☐ life-threatening
- ☐ hospitalization-initial or prolonged
- ☐ disability
- ☐ congenital anomaly
- ☐ required intervention to prevent permanent impairment/damage
- ☐ other: ____

3. Date of event (mo/day/yr)	4. Date of report (mo/day/yr)
Unk	10/31/01

5. Describe event

A 72-year-old patient received Ibuprofen and developed hypoglycemia (blood glucose less than 2.2 mmol/L) with severe nausea, sweating, palpitations and loss of consciousness.

The patient has a 20-year history of type II diabetes mellitus and his glycemic control was stable. He developed a sore throat and arthralgia and took 150 mg of Ibuprofen. Half hour later, he developed severe nausea, sweating and palpitations that immediately relieved after the patient consumed sugar. The same symptoms were reproduced again the next morning after the patient took an identical dose of Ibuprofen. After taking the same dose in the afternoon he developed the same symptoms with greater intensity and lost consciousness. The patient recovered fully soon after receiving I.V. glucose. He stopped taking Ibuprofen and has not experienced further hypoglycemic episodes.

[1] Sone H, Takahashi A, Yamada N, "Ibuprofen-Related Hypoglycemia in a Patient Receiving Sulfonylurea", Ann of Internal Med 2001; 134: 344.

6. Relevant tests/laboratory data, including dates
Unknown

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking, and alcohol use, hepatic/renal dysfunction, etc.)

Diabetes Mellitus Type II (20 yr history)
Risk Factors: Altered metabolism

C. Suspect medication(s)

1. Name (give labeled strength & mfr./labeler, if known)
1 Ibuprofen, Unk., Unk
2

2. Dose, frequency & route used	3. Therapy dates
# 1 150 mg, daily, orally	# 1 Unk
# 2	# 2

4. Diagnosis for use (indication)	5. Event abated after use stopped or dose reduced
# 1 Sore throat, arthralgia	# 1 ☒ yes ☐ no ☐ n/a
# 2	# 2 ☐ yes ☐ no ☐ n/a

6. Lot #	7. Exp. date	8. Event reappeared after reintroduction
# 1 Unk	# 1 Unk	# 1 ☐ yes ☐ no ☒ n/a
# 2	# 2	# 2 ☐ yes ☐ no ☐ n/a

9. NDC # - for product problems only (if known)
- -

10. Concomitant medical products and therapy dates (exclude treatment of event)
Unknown

D. All manufacturers

1. Contact office - name & address
Par Pharmaceutical, Inc.
One Ram Ridge Road
Spring Valley, New York 10977

2. Phone number
914-425-7100

3. Report source(s)
- ☒ foreign
- ☐ study
- ☒ literature
- ☐ consumer
- ☒ health professional
- ☐ user facility
- ☐ company representative
- ☐ distributor
- ☐ other: ____

4. Date received by manufacturer
04/25/01

5. ANDA # UNK
IND # ____
PLA # ____
pre-1938 ☐ yes
OTC Product ☐ yes

6. If IND, protocol #
N/A

7. Type of report
☐ 5-day ☒ initial
☐ 10-day ☐ 15-day
☒ periodic
☐ follow-up # ____

8. Adverse event term(s)
Hypoglycemia, Severe nausea, sweating, palpitations, loss of consciousness

9. Mfr. report #
01-136

E. Initial reporter

1. Name, address & phone number
Bayer AG
Global Product Safety (GDS)
Morristown, NJ 07962-1910 (973) 254-5000

NOV 14 2001

2. Health professional?	3. Occupation	4. Initial reporter also sent report to FDA
☒ yes ☐ no	Pharm. Co.	☐ yes ☐ no ☒ unk

FDA Form 3500A Facsimile

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

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Individual Safety Report
3825072-4-00-05

For **MANDATORY** reporting.

Page 5 of 11

Form Approved by FDA 05/13/97

Mfr. report # 01-137
UF/Dist.report #
FDA Use Only

A. Patient information

1. Patient identifier	2. Age at time of event:	3. Sex	4. Weight
Unknown in confidence	or 25 Date of birth: Unk	☒ female ☐ male	Unk lbs or _____ kgs

B. Adverse event

1. ☒ Adverse event and/or ☐ Product problem (eg. defect/malfunct.)

2. Outcomes attributed to adverse event (check all that apply)
- ☐ death _____
- ☐ life-threatening
- ☒ hospitalization-initial or prolonged
- ☐ disability
- ☐ congenital anomaly
- ☐ required intervention to prevent permanent impairment/damage
- ☐ other: _____

3. Date of event	4. Date of report
(mo/day/yr) Unk	(mo/day/yr) 10/31/01

5. Describe event

01-137

A 25 year old female was admitted to the hospital because of wheezing, dyspnea, nasal obstruction epiphora, and ear fullness. These symptoms occurred 30 minutes after the intake of 200 mg of Ibuprofen and 100 mg of Norfloxacin, which were prescribed for an upper respiratory tract infection. The patient kept 20 hamsters and a dog which were removed from her home. After removal of the animals the patient became asymptomatic without further medication and her airway hyper-responsiveness were also alleviated. The diagnosis of aspirin-induced asthma was confirmed by single-blind oral challenge with 100 mg of Ibuprofen. All previous symptoms reappeared 40 minutes after Ibuprofen intake.

[1] Kawai K, Shirai T, Suzuki K, Chida K, Nakamura H, "Mild Intermittent Aspirin-Induced Asthma in a Patient Who Became Asymptomatic After Removal of Pet Hamsters From Home" J JPN Respir Soc 2000; 38: 298-301.

6. Relevant tests/laboratory data, including dates
Unk

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking, and alcohol use, hepatic/renal dysfunction, etc.)
Seasonal rhinitis, nocturnal asthmatic symptoms
Risk factor: Allergy

C. Suspect medication(s)

1. Name (give labeled strength & mfr./labeler, if known)
1 Ibuprofen, Unk, Unk
2

2. Dose, frequency & route used	3. Therapy dates
# 1 200 mg, daily, orally	# 1 Unk
# 2	# 2

4. Diagnosis for use (indication)	5. Event abated after use stopped or dose reduced
# 1 Upper Respiratory tract infection	# 1 ☒ yes ☐ no ☐ n/a
# 2	# 2 ☐ yes ☐ no ☐ n/a

6. Lot #	7. Exp. date	8. Event reappeared after reintroduction
# 1 Unk	# 1 Unk	# 1 ☐ yes ☐ no ☒ n/a
# 2	# 2	# 2 ☐ yes ☐ no ☐ n/a

9. NDC # - for product problems only (if known)
- -

10. Concomitant medical products and therapy dates (exclude treatment of event)
Norfloxacin, 100 mg, orally

D. All manufacturers

1. Contact office - name & address
Par Pharmaceutical, Inc.
One Ram Ridge Road
Spring Valley, New York 10977

2. Phone number
914-425-7100

3. Report source(s)
- ☒ foreign
- ☐ study
- ☒ literature
- ☐ consumer
- ☒ health professional
- ☐ user facility
- ☐ company representative
- ☐ distributor
- ☐ other: _____

4. Date received by manufacturer
04/20/01

5. ANDA # UNK
IND # _____
PLA # _____
pre-1938 ☐ yes
OTC Product ☐ yes

6. If IND, protocol #
N/A

7. Type of report
- ☐ 5-day ☒ initial
- ☐ 10-day ☐ 15-day
- ☒ periodic
- ☐ follow-up # _____

8. Adverse event term(s)
Asthma, wheezing, dyspnea, epiphora, ear fullness, nasal obstruction, allergic reaction

9. Mfr. report #
01-137

E. Initial reporter

1. Name, address & phone number
Bayer AG
Global Product Safety (GDS)
Morristown, NJ 07962-1910 (973) 254-5000

NOV 1 9 2001

2. Health professional?	3. Occupation	4. Initial reporter also sent report to FDA
☒ yes ☐ no	Pharm. Co.	☐ yes ☐ no ☒ unk

FDA Form 3500A Facsimile

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Individual Safety Report
3825072-4-00-06

Form Approved by FDA 05/13/97

For **MANDATORY** reporting.

Mfr. report # 01-138
UF/Dist.report #
FDA Use Only

A. Patient information

1. Patient identifier	2. Age at time of event:	3. Sex	4. Weight
Unk in confidence	or 19 Date of birth: Unk	☒ female ☐ male	Unk lbs or ____ kgs

B. Adverse event

1. ☒ Adverse event and/or ☐ Product problem (eg, defect/malfunct.)

2. Outcomes attributed to adverse event (check all that apply)
☐ death _____
☐ life-threatening
☒ hospitalization-initial or prolonged
☐ disability
☐ congenital anomaly
☐ required intervention to prevent permanent impairment/damage
☐ other: _____

3. Date of event (mo/day/yr)	4. Date of report (mo/day/yr)
Unk	10/31/01

5. Describe event
A 19 year-old female ingested 30 Ibuprofen tablets, 800 mg and an unknown amount of a barbiturate and alcohol in a suicide attempt. The patient was lethargic but could follow verbal commands. Vital signs were blood pressure 126/70 mmHg, heart rate 120 beats/min, respiratory rate 16 breaths/min and temperature 97°F. The nasopharynx, lung and heart examinations were normal.
Gastric lavage and activated charcoal was administered. She vomited charcoal shortly after administration and began experiencing difficulty breathing and an increase in the pitch of her voice. A chest X-ray study showed a widened mediastinum, pneumopericardium and subcutaneous emphysema consistent with esophageal perforation which was confirmed by computed tomography scan. Surgical exploration revealed a tear in the proximal posterior esophagus with charcoal in the mediastinum. She remained intubated for 7 days and was discharged 14 days after admission.
[1] Caravati EM, Knight HH, Linscott MS Jr., Stringham JC, "Esophageal Laceration and Charcoal Mediastinum Complicating Gastric Lavage", J Emerg Med 2001, 20: 273-276.

6. Relevant tests/laboratory data, including dates
Unknown

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking, and alcohol use, hepatic/renal dysfunction, etc.)
Suicide attempt - intentional overdose

C. Suspect medication(s)

1. Name (give labeled strength & mfr./labeler, if known)
1 Ibuprofen, 24 G, Unknown
2

2. Dose, frequency & route used	3. Therapy dates
# 1 24 G, Orally,	# 1 Unk
# 2	# 2

4. Diagnosis for use (indication)	5. Event abated after use stopped or dose reduced
# 1 Intentional OD, Suicide Attempt	# 1 ☐ yes ☐ no ☒ n/a
# 2	# 2 ☐ yes ☐ no ☐ n/a

6. Lot #	7. Exp. date	8. Event reappeared after reintroduction
# 1 Unk	# 1 Unk	# 1 ☐ yes ☐ no ☒ n/a
# 2	# 2	# 2 ☐ yes ☐ no ☐ n/a

9. NDC # - for product problems only (if known)
- -

10. Concomitant medical products and therapy dates (exclude treatment of event)
Unknown

D. All manufacturers

1. Contact office - name & address
Par Pharmaceutical, Inc.
One Ram Ridge Road
Spring Valley, New York 10977

2. Phone number
914-425-7100

3. Report source(s)
☐ foreign
☐ study
☒ literature
☐ consumer
☒ health professional
☐ user facility
☐ company representative
☐ distributor
☐ other: _____

4. Date received by manufacturer	5.
05/20/01	ANDA # UNK IND # PLA # pre-1938 ☐ yes OTC Product ☐ yes
6. If IND, protocol # N/A	
7. Type of report ☐ 5-day ☒ initial ☐ 10-day ☐ 15-day ☒ periodic ☐ follow-up #	

8. Adverse event term(s)	9. Mfr. report #
Intentional Overdose, Suicide Attempt	01-138

E. Initial reporter

1. Name, address & phone number
Bayer AG
Global Product Safety (GDS)
Morristown, NJ 07962-1910 (973) 254-

NOV 14 2001

2. Health professional?	3. Occupation	4. Initial reporter also sent report to FDA
☒ yes ☐ no	Pharm. Co.	☐ yes ☐ no ☒ unk

FDA Form 3500A Facsimile

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

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3825072-4-00-07

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For **MANDATORY** reporting.

Page 7 of 11

Form Approved by FDA 05/13/97

Mfr. report # 01-139
UF/Dist.report #
FDA Use Only

A. Patient information

1. Patient identifier	2. Age at time of event:	3. Sex	4. Weight
Unk in confidence	or 9 months Date of birth:	☐ female ☒ male	Unk lbs or _____ kgs

B. Adverse event

1. ☒ Adverse event and/or ☐ Product problem (eg, defect/malfunct.)

2. Outcomes attributed to adverse event (check all that apply)
- ☐ death _____
- ☐ life-threatening
- ☒ hospitalization-initial or prolonged
- ☐ disability
- ☐ congenital anomaly
- ☐ required intervention to prevent permanent impairment/damage
- ☐ other: _____

3. Date of event (mo/day/yr)	4. Date of report (mo/day/yr)
Unknown	10/31/01

5. Describe event

This is an initial case of a 9 month male who received Ibuprofen and developed a perforated peptic ulcer with abdominal distension. The patient had suffered from an upper respiratory tract infection with fever for about 2 weeks and was treated intermittently with Ibuprofen.

At laparotomy, a 0.8-cm perforated hole was found over the prepyloric area. Simple closure with omental patching was performed after debridement of the perforation. Pathologic examination showed chronic peptic ulcer with helicobacter pylori infection. The postoperative course and outcome were satisfactory.

[1] Feng CY, HSU WM, Chen Y, "Perforated Peptic Ulcer in an Infant", J. Formosan Med Assoc 2001; 100: 131-133.

6. Relevant tests/laboratory data, including dates
Unknown

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking, and alcohol use, hepatic/renal dysfunction, etc.)
Chronic peptic ulcer

C. Suspect medication(s)

1. Name (give labeled strength & mfr./labeler, if known)
1 Ibuprofen Tablets, Unk, Unk
2

2. Dose, frequency & route used	3. Therapy dates
# 1 Unk	# 1 Unk
# 2	# 2

4. Diagnosis for use (indication)	5. Event abated after use stopped or dose reduced
# 1 respirtory tract infection, fever	# 1 ☐ yes ☐ no ☒ n/a
# 2	# 2 ☐ yes ☐ no ☐ n/a

6. Lot #	7. Exp. date	8. Event reappeared after reintroduction
# 1 Unk	# 1 Unk	# 1 ☐ yes ☐ no ☒ n/a
# 2	# 2	# 2 ☐ yes ☐ no ☐ n/a

9. NDC # - for product problems only (if known)
- -

10. Concomitant medical products and therapy dates (exclude treatment of event)
Unknown

D. All manufacturers

1. Contact office - name & address
Par Pharmaceutical, Inc.
One Ram Ridge Road
Spring Valley, New York 10977

2. Phone number
914-425-7100

3. Report source(s)
- ☒ foreign
- ☐ study
- ☒ literature
- ☐ consumer
- ☒ health professional
- ☐ user facility
- ☐ company representative
- ☐ distributor
- ☐ other: _____

4. Date received by manufacturer
05/22/01

5. ANDA # UNK
IND # _____
PLA # _____
pre-1938 ☐ yes
OTC Product ☐ yes

6. If IND, protocol #
N/A

7. Type of report
- ☐ 5-day ☒ initial
- ☐ 10-day ☐ 15-day
- ☒ periodic
- ☐ follow-up # _____

8. Adverse event term(s)
Perforated peptic ulcer, abdominal distension

9. Mfr. report #
01-139

E. Initial reporter

1. Name, address & phone number
Bayer AG
Global Product Safety (GDS)
Morristown, NJ 07962-1910 (973) 254-5000

NOV 14 2001

2. Health professional?	3. Occupation	4. Initial reporter also sent report to FDA
☒ yes ☐ no	Pharm. Co.	☐ yes ☐ no ☒ unk

FDA Form 3500A Facsimile

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

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Individual Safety Report

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For **MANDATORY** reporting.

Page 8 of 11

Form Approved by FDA 05/13/97

Mfr. report # 01-140
UF/Dist.report #
FDA Use Only

A. Patient information

1. Patient identifier	2. Age at time of event:	3. Sex	4. Weight
Unk in confidence	or Unk Date of birth:	☐ female ☐ male	Unk lbs or _____ kgs

B. Adverse event

1. ☒ Adverse event and/or ☐ Product problem (eg, defect/malfunct.)

2. Outcomes attributed to adverse event (check all that apply)
- ☐ death _____
- ☐ life-threatening
- ☐ hospitalization-initial or prolonged
- ☐ disability
- ☐ congenital anomaly
- ☐ required intervention to prevent permanent impairment/damage
- ☐ other: _____

3. Date of event (mo/day/yr)	4. Date of report (mo/day/yr)
Unk	10/31/01

5. Describe event

Gentamicin and standard-dose Ibuprofen were administered to an adolescent with cystic fibrosis who developed renal failure and severe vestibulotoxicity. A contributing factor was a possible suboptimal intravascular volume status.

Author felt that because of the potential severity of this drug interaction, hydration status and renal and vestibular functions should be closely monitored in patients received ibuprofen and intravenous aminoglycosides concomitantly.

[1] Scott CS, Retsch-Bogart GZ, Henry MM. "Renal failure and vestibular Toxicity in an Adolescent with Cystic Fibrosis Receiving Gentamicin and Standard-Dose Ibuprofen", Pediatr Pulmonol 2001; 31: 314-316.

6. Relevant tests/laboratory data, including dates

Unknown

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking, and alcohol use, hepatic/renal dysfunction, etc.)

Unknown

C. Suspect medication(s)

1. Name (give labeled strength & mfr./labeler, if known)

1 Ibuprofen, Unk, Unk

2

2. Dose, frequency & route used	3. Therapy dates
# 1 Unknown	# 1 Unknown
# 2	# 2

4. Diagnosis for use (indication)	5. Event abated after use stopped or dose reduced
# 1 Cystic Fibrosis	# 1 ☐ yes ☐ no ☒ n/a
# 2	# 2 ☐ yes ☐ no ☐ n/a

6. Lot #	7. Exp. date	8. Event reappeared after reintroduction
# 1 Unk	# 1 Unk	# 1 ☐ yes ☐ no ☒ n/a
# 2	# 2	# 2 ☐ yes ☐ no ☐ n/a

9. NDC # - for product problems only (if known)

\- -

10. Concomitant medical products and therapy dates (exclude treatment of event)

Gentamicin

D. All manufacturers

1. Contact office - name & address

Par Pharmaceutical, Inc.
One Ram Ridge Road
Spring Valley, New York 10977

2. Phone number 914-425-7100

3. Report source(s)
- ☐ foreign
- ☐ study
- ☒ literature
- ☐ consumer
- ☒ health professional
- ☐ user facility
- ☐ company representative
- ☐ distributor
- ☐ other: _____

4. Date received by manufacturer	5.
05/21/01	ANDA # UNK IND # _____ PLA # _____ pre-1938 ☐ yes OTC Product ☐ yes
6. If IND, protocol # N/A	
7. Type of report ☐ 5-day ☒ initial ☐ 10-day ☐ 15-day ☒ periodic ☐ follow-up # _____	

8. Adverse event term(s)	9. Mfr. report #
Renal Failure, Vestibulotoxicity	01-140

E. Initial reporter

1. Name, address & phone number

Bayer AG
Global Product Safety (GDS)
Morristown, NJ 07962-1910 (973) 254-5000

NOV 14 2001

2. Health professional?	3. Occupation	4. Initial reporter also sent report to FDA
☒ yes ☐ no	Pharm. Co.	☐ yes ☐ no ☒ unk

FDA Form 3500A Facsimile

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Individual Safety Report
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For **MANDATORY** reporting.

Page 9 of 11

Form Approved by FDA 05/13/97

Mfr. report # 01-141
UF/Dist.report #
FDA Use Only

A. Patient information

1. Patient identifier	2. Age at time of event:	3. Sex	4. Weight
Unknown in confidence	or 12 Date of birth:	☒ female ☐ male	Unk lbs or _____ kgs

B. Adverse event

1. ☒ Adverse event and/or ☐ Product problem (eg, defect/malfunct.)

2. Outcomes attributed to adverse event (check all that apply)
- ☐ death _____
- ☐ life-threatening
- ☒ hospitalization-initial or prolonged
- ☐ disability
- ☐ congenital anomaly
- ☐ required intervention to prevent permanent impairment/damage
- ☐ other: _____

3. Date of event (mo/day/yr)	4. Date of report (mo/day/yr)
Unknown	10/31/01

5. Describe event

The case describes a 12-year-old female patient with cystic fibrosis who received ibuprofen and developed pyloric channel stricture.

The patient started taking 1000 mg generic ibuprofen, twice daily, to treat the pulmonary manifestations of cystic fibrosis in 1996. Soon after her clinical visit the patient developed emesis and intolerance of solid foods which persisted for several months and resulted in weight loss of 7 kilograms. She was referred to a pediatric gastroenterologist, who performed an upper endoscopy and subsequently diagnosed a pyloric channel structure. The patient was admitted to the hospital. The patient's pyloric channel stricture dilated with two balloons. No active ulcer was noted upon dilation. The patient wad advanced to a regular soft diet and discharged 2 days later. Omeprazole 20 mg/d was added to her maintenance cystic fibrosis medications. Ibuprofen, cisapride and ranitidine were discontinued. Over the course of the following year, the patient was asymptomatic.

[1] Bell ES, Grothe R, Zivkovich V et al, "Pyloric channel Stricture Secondary to High-Dose Ibuprofen Therapy in a Patient with Cystic Fibrosis", Ann Pharmacother 1999; 33: 693-696

6. Relevant tests/laboratory data, including dates
Unk

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking, and alcohol use, hepatic/renal dysfunction, etc.)
Cystic Fibrosis

C. Suspect medication(s)

1. Name (give labeled strength & mfr./labeler, if known)
1 Ibuprofen, Unk, Unk
2

2. Dose, frequency & route used	3. Therapy dates
# 1 2000 MG	# 1 09/20/96 - 02/97
# 2	# 2

4. Diagnosis for use (indication)	5. Event abated after use stopped or dose reduced
# 1 Cysic Fibrosis	# 1 ☐ yes ☐ no ☒ n/a
# 2	# 2 ☐ yes ☐ no ☐ n/a

6. Lot #	7. Exp. date	8. Event reappeared after reintroduction
# 1 Unk	# 1 Unk	# 1 ☐ yes ☐ no ☒ n/a
# 2	# 2	# 2 ☐ yes ☐ no ☐ n/a

9. NDC # - for product problems only (if known)
- -

10. Concomitant medical products and therapy dates (exclude treatment of event)
Pancrelipase

D. All manufacturers

1. Contact office - name & address

Par Pharmaceutical, Inc.
One Ram Ridge Road
Spring Valley, New York 10977

2. Phone number
914-425-7100

3. Report source(s)
- ☐ foreign
- ☐ study
- ☒ literature
- ☐ consumer
- ☒ health professional
- ☐ user facility
- ☐ company representative
- ☐ distributor
- ☐ other: _____

4. Date received by manufacturer	5.
06/29/01	ANDA # UNK IND # _____ PLA # _____ pre-1938 ☐ yes OTC Product ☐ yes
6. If IND, protocol # N/A	
7. Type of report ☐ 5-day ☒ initial ☐ 10-day ☐ 15-day ☒ periodic ☐ follow-up # _____	

8. Adverse event term(s)	9. Mfr. report #
Pyloric Channel Stricture	01-141

E. Initial reporter

1. Name, address & phone number
Bayer AG
Global Product Safety (GDS)
Morristown, NJ 07962-1910 (973) 254-5000

NOV 14 2001

2. Health professional?	3. Occupation	4. Initial reporter also sent report to FDA
☒ yes ☐ no	Pharm. Co.	☐ yes ☐ no ☒ unk

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For **MANDATORY** reporting.

Page 10 of 11

Mfr. report # 01-142
UF/Dist.report #
FDA Use Only

A. Patient information

1. Patient identifier	2. Age at time of event:	3. Sex	4. Weight
Unk in confidence	or 24 months Date of birth: Unk	☒ female ☐ male	Unk lbs or _____ kgs

B. Adverse event

1. ☒ Adverse event and/or ☐ Product problem (eg, defect/malfunct.)

2. Outcomes attributed to adverse event (check all that apply)
- ☐ death _____
- ☐ life-threatening
- ☒ hospitalization-initial or prolonged
- ☐ disability
- ☐ congenital anomaly
- ☐ required intervention to prevent permanent impairment/damage
- ☐ other: _____

3. Date of event (mo/day/yr)	4. Date of report (mo/day/yr)
Unk	10/31/01

5. Describe event

This case describes a 2-year old female child who received Ibuprofen and developed Stevens-Johnson Syndrome/toxic epidermal necrolysis. The child has a skin eruption 15 days after ibuprofen intake. Examination 4 days after the eruption revealed vesicles, spots, flat atypical targets, and full-thickness epidermal detachment over the lumbar area, anterior trunk, distal superior limbs, and face leaving a purple-red oozing dermis. About 25% of the body surface was involved.

Bacterial cultures were negative at onset. A skin biopsy revealed an intra-epidermal bulla with necrotic keratinocytes at blister margins and spares perivascular lymphocytic infiltrates in the upper dermis.

The patient was admitted and initiated on pentoxifylline 12 mg/kg/day intravenously three times a day, with no further extension of epidermal necrosis. By the 7th day, re-epithelialization was complete and 17 days after parenteral pentoxifylline, she was discharged and switched to the oral medication at the same dose for 3 more weeks. One month later she was free of lesions.

[1] Sanclemente G, Roche Ca De la, Escobar CE, Falabella R, "Pentoxyfylline in Toxic Epidermal Necrolysis and Stevens-Johnson Syndrome", Int J Dermatol 1999; 38: 878-879.

6. Relevant tests/laboratory data, including dates
Unk

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking, and alcohol use, hepatic/renal dysfunction, etc.)
Unknown

C. Suspect medication(s)

1. Name (give labeled strength & mfr./labeler, if known)
1 Ibuprofen, Unk, Unk
2

2. Dose, frequency & route used	3. Therapy dates
# 1 Unk	# 1 Unk
# 2	# 2

4. Diagnosis for use (indication)	5. Event abated after use stopped or dose reduced
# 1 Unk	# 1 ☐ yes ☐ no ☒ n/a
# 2	# 2 ☐ yes ☐ no ☐ n/a

6. Lot #	7. Exp. date	8. Event reappeared after reintroduction
# 1 Unk	# 1 Unk	# 1 ☐ yes ☐ no ☒ n/a
# 2	# 2	# 2 ☐ yes ☐ no ☐ n/a

9. NDC # - for product problems only (if known)
- -

10. Concomitant medical products and therapy dates (exclude treatment of event)
Unk

D. All manufacturers

1. Contact office - name & address
Par Pharmaceutical, Inc.
One Ram Ridge Road
Spring Valley, New York 10977

2. Phone number
914-425-7100

3. Report source(s)
- ☒ foreign
- ☐ study
- ☒ literature
- ☐ consumer
- ☒ health professional
- ☐ user facility
- ☐ company representative
- ☐ distributor
- ☐ other: _____

4. Date received by manufacturer	5.
07/02/01	ANDA # UNK IND # _____ PLA # _____ pre-1938 ☐ yes OTC Product ☐ yes
6. If IND, protocol # N/A	
7. Type of report ☐ 5-day ☒ initial ☐ 10-day ☐ 15-day ☒ periodic ☐ follow-up # _____	

8. Adverse event term(s)	9. Mfr. report #
Stevens-Johnson Syndrome, Toxic Epidermal Necrolysis	01-142

E. Initial reporter

1. Name, address & phone number
Bayer AG
Global Product Safety (GDS)
Morristown, NJ 07962-1910 (973) 254-5000

NOV 1 4 2001

2. Health professional?	3. Occupation	4.Initial reporter also sent report to FDA
☒ yes ☐ no	Pharm. Co.	☐ yes ☐ no ☒ unk

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Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

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Individual Safety Report

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For **MANDATORY** reporting.

Page 11 of 11

Form Approved by FDA 05/13/97

Mfr. report # 01-143
LF/Dist.report #
FDA Use Only

A. Patient information

1. Patient identifier	2. Age at time of event:	3. Sex	4. Weight
Unk in confidence	or 82 Date of birth: Unk	☒ female ☐ male	Unk lbs or _____ kgs

B. Adverse event

1. ☒ Adverse event and/or ☐ Product problem (eg, defect/malfunct.)

2. Outcomes attributed to adverse event (check all that apply)

☒ death _____
☐ life-threatening
☐ hospitalization-initial or prolonged
☐ disability
☐ congenital anomaly
☐ required intervention to prevent permanent impairment/damage
☐ other: _____

3. Date of event (mo/day/yr)	4. Date of report (mo/day/yr)
Unk	10/31/01

5. Describe event

An 82 year-old female patient was admitted to the hospital by her general practitioner with anemia. She complained of generalized aches and pains from flu, for which she had been taking over-the-counter Ibuprofen 1200 mg daily for 10 days. This medication was stopped on admission.

Two days prior to the admission she became increasingly nauseous and vomited twice. There was no history of hematemesis or melena. Her past medical history consisted of hypertension and chronic renal impairment (secondary to renal artery stenosis), angina, mild left ventricular failure, gout and osteoarthritis.

Her hemoglobin on admission was 6.5 g/dl and she was transfused 4 units of blood. Two days later it was noticed that she began passing black stools and an upper gastrointestinal endoscopy was carried out which demonstrated altered blood in the duodenum. She was treated with a proton pump inhibitor. The following day her hemoglobin dropped to 5.8 g/dl after 3 further episodes of melena and she became clinically shocked. After numerous transfusions and inotropic support the patient unfortunately passed away.

A post mortem was carried out which demonstrated hemorrhagic duodenitis and gastritis presumed secondary to the ibuprofen ingestion. There was no evidence of helicobacter pylori infection.

6. Relevant tests/laboratory data, including dates

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking, and alcohol use, hepatic/renal dysfunction, etc.)

Hypertension, chronic renal impairment, angina, mild L ventricular failure, gout osteoarthritis, renal artery stenosis

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C. Suspect medication(s)

1. Name (give labeled strength & mfr./labeler, if known)

1 Ibuprofen, unk, unk

2

2. Dose, frequency & route used	3. Therapy dates
# 1 1200 mg/daily, orally	# 1 Unk
# 2	# 2

4. Diagnosis for use (indication)	5. Event abated after use stopped or dose reduced
# 1 general aches & pains from flu	# 1 ☐ yes ☐ no ☒ n/a
# 2	# 2 ☐ yes ☐ no ☐ n/a

6. Lot #	7. Exp. date	8. Event reappeared after reintroduction
# 1 Unk	# 1 Unk	# 1 ☐ yes ☐ no ☒ n/a
# 2	# 2	# 2 ☐ yes ☐ no ☐ n/a

9. NDC # - for product problems only (if known)

- -

10. Concomitant medical products and therapy dates (exclude treatment of event)

Unknown

D. All manufacturers

1. Contact office - name & address

Par Pharmaceutical, Inc.
One Ram Ridge Road
Spring Valley, New York 10977

2. Phone number 914-425-7100

3. Report source(s)
☒ foreign
☐ study
☒ literature
☐ consumer
☒ health professional
☐ user facility
☐ company representative
☐ distributor
☐ other: _____

4. Date received by manufacturer 09/13/01

5. ANDA # UNK
IND # _____
PLA # _____
pre-1938 ☐ yes
OTC Product ☐ yes

6. If IND, protocol # N/A

7. Type of report
☐ 5-day ☒ initial
☐ 10-day ☐ 15-day
☒ periodic
☐ follow-up # _____

8. Adverse event term(s)

Hemorrhagic duodenitis, hemoglobin decrease, black stools, gastritis, vomitting, nausea

9. Mfr. report # 01-143

E. Initial reporter

1. Name, address & phone number

Bayer AG
Global Product Safety (GDS)
Morristown, NJ 07962-1910 (973) 254-5000

NOV 14 2001

2. Health professional?	3. Occupation	4. Initial reporter also sent report to FDA
☒ yes ☐ no	Pharm. Co.	☐ yes ☐ no ☒ unk

Serious Toxicity in a Young Child Due to Ibuprofen

ELIF E. ÖKER, MD, LUKE HERMANN, MD, CARL R. BAUM, MD, KATHLEEN M. FENTZKE, MD, TODD SIGG, PHARMD, JERROLD B. LEIKIN, MD

Abstract. An 18-month-old male presented to the emergency department (ED) for evaluation of lethargy and apnea. Four hours before presentation, the patient was found with an empty bottle of ibuprofen, an ingestion of as much as 7.2 grams (600 mg/kg). The ED course was remarkable for a 30-second tonic–clonic seizure. Laboratory analysis was notable for metabolic acidosis. Four-hour and 7.5-hour serum ibuprofen levels were 640 and 39 μg/mL, respectively. Following treatment, the patient improved and was extubated the next morning. While metabolic acidosis has been frequently described at doses exceeding 400 mg/kg, seizures occurring early in the course of ibuprofen toxicity have been rarely noted. Key words: ibuprofen; poisoning; pediatrics. ACADEMIC EMERGENCY MEDICINE 2000; 7:821–823

Ibuprofen is a commonly used over-the-counter nonsteroidal anti-inflammatory analgesic derived from propionic acid. In general, overdoses of ibuprofen result in mild effects. These effects include abdominal pain, nausea, vomiting, lethargy, headache, tinnitus, and ataxia.[1] Serious toxicity, including coma, apnea, metabolic acidosis, hypotension, bradycardia, and renal and hepatic dysfunction, has been observed in ingestions of more than 400 mg/kg. Symptoms usually develop within four hours of ingestion.[1–5] We describe a child who developed severe symptoms (seizure, metabolic acidosis, apnea, and lethargy) after an ibuprofen ingestion of up to 600 mg/kg. The symptoms resolved in approximately eight hours with no long-term sequelae to date.

CASE REPORT

An 18-month-old, 12-kg male with an unremarkable past medical history was brought to the emergency department (ED) for evaluation of lethargy. According to the parents, the patient was found approximately four hours prior to presentation with an empty bottle of ibuprofen, and with pill fragments in his mouth. The patient had two episodes of emesis; one spontaneous and the other manually induced by a grandparent. After a brief period of relatively normal behavior, the parents noted that the patient became limp and was not easily aroused. The patient subsequently became apneic, prompting the parents to bring him to the ED. The patient's past medical history included eczema and otitis media. His parents indicated that he was occasionally given pseudoephedrine but was not given any in the last 24 hours. Further, it was discovered that his grandmother took lisinopril, for which all tablets were accounted. Later investigation indicated a potential ingestion of as much as 7.2 grams of ibuprofen (600 mg/kg).

On presentation to the ED, the patient was lethargic. Vital signs were: temperature (rectal) 96.8°F, respiratory rate 16 breaths/min, heart rate 125 beats/min, and blood pressure 118/48 mm Hg. The patient's vital signs remained in this range throughout his ED course. Physical exam was significant for an intact gag reflex, reactive pupils (6 mm), and withdrawal from painful stimuli. He received, in increments, a total of 600 mL of normal saline and 1 mg of naloxone without response. A short time later the patient sustained a 30-second tonic–clonic seizure, which resolved with lorazepam 1 mg IV push. The patient then became apneic, requiring endotracheal intubation. Subsequent lavage with a 12-Fr nasogastric tube and 300 mL of normal saline revealed small pill fragments. Activated charcoal was then administered. A sodium bicarbonate bolus of 12 mEq was administered, followed by an infusion of D_5W and 24 mEq/L sodium bicarbonate at 90 mL per hour, in light of the patient's persistent acidosis.

Laboratory analysis was notable for arterial blood gas pH of 7.20, pCO_2 of 39 torr, pO_2 of 469 torr, and HCO_3^- of 15 mEq/L on 100% oxygen. A second arterial blood gas, drawn approximately one hour after the first, demonstrated a pH of 7.29, pCO_2 of 80 torr, pO_2 of 336 torr, and HCO_3^- of 14 mEq/L. Serum chemistry obtained during the same period revealed Na^+ 140 mEq/L, Cl^- 107 mEq/L, HCO_3^- 17 mEq/L, K^+ 4.9 mEq/L, BUN 13 mg/dL, Cr 0.4 mg/dL, and glucose 157 mg/dL. The complete blood count was unremarkable, and serum salicylate, acetaminophen, and ethanol levels were negative; urine toxicology screen was negative for cocaine, phencyclidine, opiates, benzodiazepines, barbiturates, and cannabinoids. An electrocardiogram demonstrated a sinus rhythm without QRS prolongation. A four-hour serum ibuprofen level was 640 μg/mL.

The patient was then transferred to a tertiary care children's hospital. A blood gas obtained after transfer demonstrated a pH of 7.26, while concomitant serum chemistry showed bicarbonate of 18.2 mEq/L

From the Department of Emergency Medicine, University of Illinois at Chicago (EEO); Department of Emergency Medicine, Cook County Hospital (LH); Department of Pediatrics, Northwestern University Medical Center/Children's Memorial Hospital (KMF, CRB); Department of Internal Medicine, Rush–Presbyterian-St-Luke's Medical Center (JBL); Toxikon Consortium (EEO, CRB, JBL); and Illinois Poison Center (TS), Chicago, Illinois.

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Address for correspondence and reprints: Elif E. Öker, MD, Department of Emergency Medicine, University of Illinois at Chicago, 1740 West Taylor Street, Suite 1600, Chicago, IL 60612. Fax: 312-996-2727; e-mail: istan_bul@msn.com

though these researchers also proposed the acquired pathogenesis of duodenal diaphragms, it is unclear as to whether nonsteroidal antiinflammatory drugs were an etiologic factor.

Several possible differential diagnoses include duodenal strictures that result from other causes such as potassium-induced stricture or neoplastic, ischemic, inflammatory (e.g., Crohn's disease), and infectious (e.g., tuberculosis) causes, all of which could be excluded on clinical and pathologic grounds.

Duodenal diaphragms are difficult to diagnose preoperatively, and even at laparotomy, unless duodenotomy with digital exploration of the lumen is performed because the thin diaphragm cannot be detected by palpation of the intact duodenum. Upper gastrointestinal series or hypotonic duodenography, which can give a high diagnostic yield, can show complete or incomplete obstruction at the duodenum; when barium passes through the eccentric opening, the wall of the diaphragm can be identified as a lucent line on these studies. However, a radiologist can also miss the duodenal diaphragm if the diaphragm resembles exaggerated mucosal folds.

Sung Eun Rha
Jae Hee Lee
Sung Yong Lee
Seung Man Park
Our Lady of Mercy Hospital
The Catholic University of Korea
Inchon 403-010, South Korea

References

1. Ferraris VA, McPhail JF. Adult duodenal web associated with peptic ulcer disease. *Surg Gynecol Obstet* 1984;158:461–463
2. Kanaan S, McGreevy PS, Fallenon TE. Nonsteroidal anti-inflammatory drug induced duodenal web. *S D J Med* 1997;50:393–394
3. Blinder CH, Haveleeele ML, Hofvaut JP, Kocka MM, Hubens HKL. Duodenal diaphragmlike structure induced by acetylsalicylic acid. *Dig Dis Sci* 1994;39:1365–1369
4. Going JJ, Garvin J, Sturrock R. Possible precursor of diaphragm disease in the small intestine. *Lancet* 1993;341:638–639
5. Bilbao MK, Frischke LH, Resch J, Benson JA Jr, Dotter CT. Postbulbar duodenal ulcer and ring-stricture. *Radiology* 1971;100:27–35

CT Detection of Tracheobronchial Calcification in an 18-Year-Old on Maintenance Warfarin Sodium Therapy: Cause and Effect?

Calcification of tracheobronchial cartilage on chest radiographs has long been recognized as an age-related phenomenon [1]. Although CT has been shown to be more sensitive to the presence of tracheobronchial calcification than conventional radiography [2], this finding is still age-related, occurring almost exclusively in patients who are more than 40 years old. We report a case of tracheobronchial calcification on CT in an 18-year-old woman receiving long-term warfarin sodium therapy.

An 18-year-old woman with a history of congenital mitral valve regurgitation presented with increasing dyspnea and exercise intolerance. Because she had undergone mitral valve replacement at age 14 months and again at 11 years, she had received long-term warfarin sodium therapy. In addition, she had been treated for ventricular ectopy with amiodarone for the past 3 years. Recent declines in pulmonary function test results and cardiac catheterization findings of pulmonary arterial hypertension prompted a high-resolution CT examination of the chest to exclude drug-induced pulmonary interstitial fibrosis. CT failed to reveal any interstitial lung disease but clearly showed the incidental finding of tracheobronchial cartilage calcification (Fig. 3), which could easily have been missed on a chest radiograph obtained the same day.

During the past 15 years, two articles have reported tracheobronchial cartilage calcification on chest radiographs of children who had undergone mitral valve replacement surgery. In these reports, four of five patients were known to be treated with warfarin sodium, implicating the drug as an etiologic agent [3, 4]. Subsequent work showed an increased incidence of tracheobronchial calcification in adults receiving warfarin sodium versus that in age-matched control subjects (47% versus 19%, respectively) [5].

The mechanism of warfarin sodium–induced tracheobronchial cartilage calcification remains obscure because it is also a normal age-related process. However, because warfarin embryopathy manifests as calcifications in and around joints and airway and nasal cartilages, it is possible that the mechanisms of these two entities are related. Researchers studying rats have found calcification of cartilage and elastic connective tissue in animals maintained on warfarin [6–8]. These findings support the hypothesis that warfarin inhibits normal formation of a vitamin K–dependent protein that prevents calcification of cartilage and connective tissue.

As more CT examinations are performed on younger patients receiving warfarin, more cases of tracheobronchial calcification will be seen. Radiologists should realize that this finding is not normal in pediatric or young adult patients and should be aware of its association with warfarin sodium therapy.

Aparna Joshi
Walter E. Berdon
Carrie Ruzal-Shapiro
Robyn J. Barst
Babies and Children's Hospital of New York
Columbia-Presbyterian Medical Center
New York, NY 10032

References

1. Brown SM, Stark P, Jacobson F. Tracheobronchial calcifications in an inpatient population. *J Thorac Imaging* 1995;10:220–222

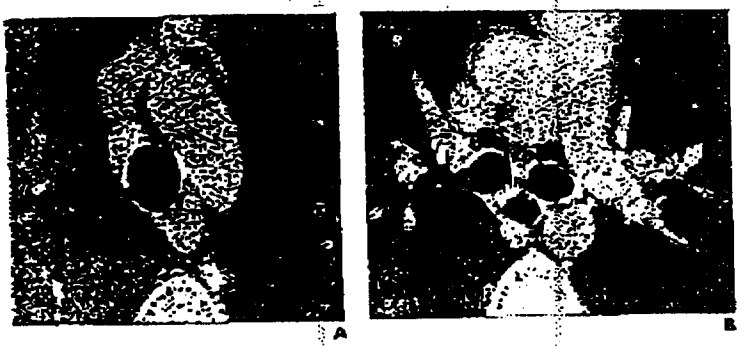

Fig. 3.—18-year-old woman on long-term warfarin sodium therapy after mitral valve replacement.
A and B, Unenhanced CT scans of chest show calcification of tracheal (A) and bronchial (B; cartilage.

infection, especially with *Escherichia coli*, is strongly associated with this entity [2].

Multiphasic contrast-enhanced dynamic MR imaging was effective in depicting the disappearance of the corticomedullary junction and multiple small nodular lesions in the kidney, thus revealing the diffuse distribution of the disease. Images obtained using this technique may provide a better understanding of the distribution of the multinodular type of renal malacoplakia and may increase its radiologic prevalence.

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Hitomi Awaya
Donald G. Mitchell
Thomas Jefferson University Hospital
Philadelphia, PA 19107

References

1. Von Hansemann D. Uber malakoplakie der harnblase. *Virchows Arch* 1903;173:302
2. Dobyan DC, Thurong LD, Ekunoyan G. Renal malacoplakia reappraised. *Am J Kidney Dis* 1993; 22:243–252

Duodenal Diaphragm Associated with Long-Term Use of Nonsteroidal Antiinflammatory Drugs: A Rare Cause of Duodenal Obstruction in an Adult

Duodenal diaphragm or web in an adult is a rare disease with congenital and acquired causes. In patients with congenital duodenal diaphragm, the obstructive symptoms usually occur during infancy, but the onset of symptoms begins during adulthood in approximately 30–35% of the patients [1]. To the contrary, multiple diaphragms in the small bowel are acquired lesions that are usually caused by the long-term use of nonsteroidal antiinflammatory drugs. In fact, diaphragms occurring at the duodenum and small intestine are macroscopically and microscopically similar to each other; therefore, some researchers [2, 3] proposed the same pathogenesis. Although a number of cases of small-intestinal diaphragms due to long-term use of nonsteroidal antiinflammatory drugs have been reported in the literature, no reports regarding the duodenal diaphragm associated with nonsteroidal antiinflammatory drugs in an adult have been published in the radiology literature, to the best of our knowledge.

A 55-year-old man presented to our hospital for surgical treatment of avascular necrosis of both hips. He had been using nonsteroidal antiinflammatory drugs and steroids (piroxicam, ibuprofen, and betamethasone) for 4 years to relieve hip joint pain. In addition to complaining of hip joint pain, he began to complain of epigastric pain with a duration of 1 month. Therefore, endoscopy was performed 1 month before hospital admission, revealing an active ulceration in the prepyloric antrum; at that time, there was no evidence of duodenal obstruction. At admission, the patient complained of frequent nonbilious vomiting. Upper gastrointestinal series revealed smooth narrowing of the pyloric canal and marked distension of the first and second portion of the duodenum (Fig. 2A). On a 45-min delayed compression spot radiograph, a longitudinal diaphragm was visualized at the obstructed site, causing severe delay of barium passage to the distal duodenum (Fig. 2B).

Exploratory laparotomy was performed to relieve the patient's symptoms. Duodenotomy revealed an incomplete 3-mm-thick diaphragm at the third portion of the duodenum, which was a membranous type with a central tiny aperture. Adjacent duodenal mucosa was markedly edematous. During surgery, total excision of the diaphragm and subtotal gastrectomy were performed. The patient was discharged from the hospital and had an uneventful recovery with complete relief of obstructive symptoms.

The precise pathogenesis of small-bowel diaphragms caused by long-term use of nonsteroidal antiinflammatory drugs is not certain, but Going et al. [4] suggested that circumferential ulceration in the small intestine might be the precursor of intestinal diaphragms. The submucosal granulation tissue of the healing ulcer matures into collagenous scar tissue that contracts to create the webs or diaphragms. The small-intestinal diaphragms caused by long-term use of nonsteroidal antiinflammatory drugs and duodenal diaphragms are similar macroscopically and microscopically [2]. In both cases, diaphragms are formed by the mucosa and submucosa of affected bowels without evidence of scarring or thickening on the serosal surface. Therefore, some researchers [2, 3] proposed that the acquired pathogenesis is related to nonsteroidal antiinflammatory drug ingestion. In 1971, Bilbao et al. [5] described a large series of 12 duodenal strictures of the descending duodenum seen with postbulbar duodenal ulcers. Al-

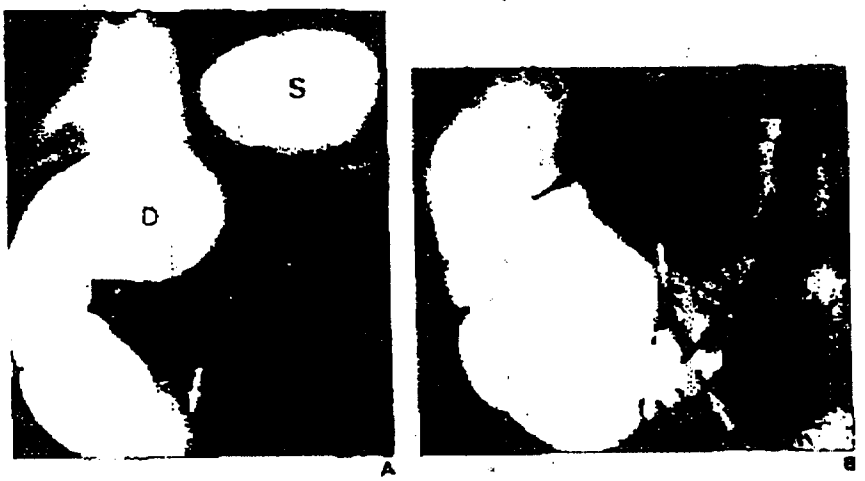

Fig. 2.—55-year-old man with duodenal diaphragm.
A, Upper gastrointestinal radiograph shows smooth narrowing of pyloric canal and marked distention of first and second portion of duodenum (D). Also, note marked passage disturbance at third portion of duodenum to distal bowel loops (*arrows*). S = stomach.
B, Compression spot radiograph obtained with 45-min delay shows longitudinal radiolucent line (*arrows*) at obstructed site, mimicking exaggerated mucosal fold.

though these researchers also proposed the acquired pathogenesis of duodenal diaphragms, it is unclear as to whether nonsteroidal antiinflammatory drugs were an etiologic factor.

Several possible differential diagnoses include duodenal strictures that result from other causes such as potassium-induced stricture or neoplastic, ischemic, inflammatory (e.g., Crohn's disease), and infectious (e.g., tuberculosis) causes, all of which could be excluded on clinical and pathologic grounds.

Duodenal diaphragms are difficult to diagnose preoperatively, and even at laparotomy, unless duodenotomy with digital exploration of the lumen is performed because the thin diaphragm cannot be detected by palpation of the intact duodenum. Upper gastrointestinal series or hypotonic duodenography, which can give a high diagnostic yield, can show complete or incomplete obstruction at the duodenum; when barium passes through the eccentric opening, the wall of the diaphragm can be identified as a linear line on these studies. However, a radiologist can also miss the duodenal diaphragm if the diaphragm resembles exaggerated mucosal folds.

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Our Lady of Mercy Hospital
The Catholic University of Korea
Inchon 403-016, South Korea

References

1. Ferreris VA, McPhail JF. Adult duodenal web associated with peptic ulcer disease. *Surg Gynecol Obstet* 1984;158:461–463
2. Kamran S, McGreevy PS, Fullerton TE. Nonsteroidal anti-inflammatory drug induced duodenal web. *S D J Med* 1997;50:393–394
3. Blieden GH, Rauschecker ML, Holvoet JP, Kocka MM, Mahens EKL. Duodenal diaphragm-like stricture induced by acetylsalicylic acid. *Dig Dis Sci* 1994;39:1365–1369
4. Going JJ, Carvin J, Stormark R. Possible precursor of diaphragm disease in the small intestine. *Lancet* 1993;341:638–639
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CT Detection of Tracheobronchial Calcification in an 18-Year-Old on Maintenance Warfarin Sodium Therapy: Cause and Effect?

Calcification of tracheobronchial cartilage on chest radiographs has long been recognized as an age-related phenomenon [1]. Although CT has been shown to be more sensitive to the presence of tracheobronchial calcification than conventional radiography [2], this finding is still age-related, occurring almost exclusively in patients who are more than 40 years old. We report a case of tracheobronchial calcification on CT in an 18-year-old woman receiving long-term warfarin sodium therapy.

An 18-year-old woman with a history of congenital mitral valve regurgitation presented with increasing dyspnea and exercise intolerance. Because she had undergone mitral valve replacement at age 14 months and again at 11 years, she had received long-term warfarin sodium therapy. In addition, she had been treated for ventricular ectopy with amiodarone for the past 3 years. Recent declines in pulmonary function test results and cardiac catheterization findings of pulmonary arterial hypertension prompted a high-resolution CT examination of the chest to exclude drug-induced pulmonary interstitial fibrosis. CT failed to reveal any interstitial lung disease but clearly showed the incidental finding of tracheobronchial cartilage calcification (Fig. 3), which could easily have been missed on a chest radiograph obtained the same day.

During the past 15 years, two articles have reported tracheobronchial cartilage calcification on chest radiographs of children who had undergone mitral valve replacement surgery. In these reports, four of five patients were known to be treated with warfarin sodium, implicating the drug as an etiologic agent [3, 4]. Subsequent work showed an increased incidence of tracheobronchial calcification in adults receiving warfarin sodium versus that in age-matched control subjects (47% versus 19%, respectively) [5].

The mechanism of warfarin sodium–induced tracheobronchial cartilage calcification remains obscure because it is also a normal age-related process. However, because warfarin embryopathy manifests as calcifications in and around joints and airway and nasal cartilages, it is possible that the mechanisms of these two entities are related. Researchers studying rats have found calcification of cartilage and elastic connective tissue in animals maintained on warfarin [6–8]. These findings support the hypothesis that warfarin inhibits normal formation of a vitamin K–dependent protein that prevents calcification of cartilage and connective tissue.

As more CT examinations are performed on younger patients receiving warfarin, more cases of tracheobronchial calcification will be seen. Radiologists should realize that this finding is not normal in pediatric or young adult patients and should be aware of its association with warfarin sodium therapy.

Aparna Joshi
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Carrie Ruzal-Shapiro
Robyn J. Bazi
Babies and Children's Hospital of New York
Columbia-Presbyterian Medical Center
New York, NY 10032

References

1. Brave SM, Stark P, Jacobson F. Tracheobronchial calcifications in an inpatient population. *J Thorac Imaging* 1995;10:220–222

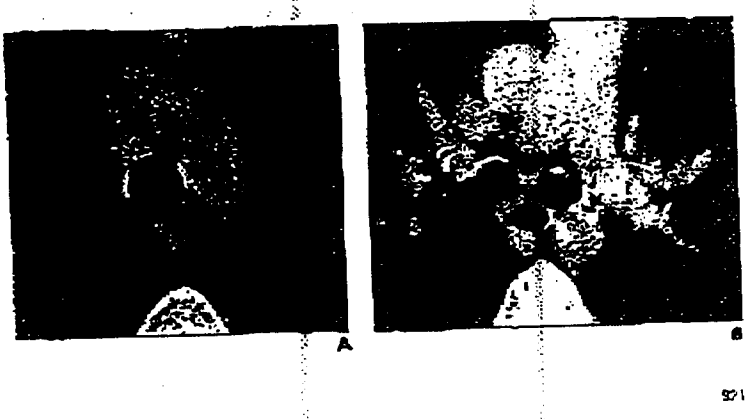

Fig. 3.—18-year-old woman on long-term warfarin sodium therapy after mitral valve replacement.
A and B, Unenhanced CT scans of chest show calcification of tracheal (A) and bronchial (B) cartilage.

3848262-3-00-01

MEDWATCH

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

Approved by FDA on 3/22/94

Corporation

Mfr report # 200111977BCC

Page 1 of 3

FDA Use Only

A. Patient information

1. Patient identifier [redacted] in confidence
2. Age at time of event: 36 yrs or Date of birth: [redacted]
3. Sex: female / male
4. Weight: 190 lbs or kgs

B. Adverse event or product problem

1. Adverse event and/or Product problem (e.g., defects/malfunctions)
2. Outcomes attributed to adverse event (check all that apply)
   - death (mo-day-yr)
   - life-threatening
   - hospitalization - initial or prolonged
   - disability
   - congenital anomaly
   - required intervention to prevent permanent impairment/damage
   - other: Med.Important
3. Date of event (mo-day-yr): 28-SEP-2001
4. Date of this report (mo-day-yr): 19-DEC-2001
5. Describe event or problem

SHAKINESS
BEGAN TO SWEAT
STOMACH PAIN
STOMACH BLEEDING
Blood in stool

Global narrative:
This initial spontaneous report was provided by a consumer via a Consumer Care Representative in the United States, and was received on 01-OCT-2001.

A 36 year old male patient of unknown race was treated with ALEVE SINUS & HEADACHE CAPLETS-10S (naproxen sodium 220 mg/ pseudoephedrine HCl 120 mg) for the indication of sinus headache at a dose of *

6. Relevant tests/laboratory data, including dates

None reported

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

Race: UNK
Pregnant: NA

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
   - #1 Aleve Sinus & Headache Caplets
   - #2 Advil (IBUPROFEN)
2. Dose, frequency & route used
   - #1 *
   - #2 *
3. Therapy dates (if unknown, give duration) (mo-day-yr or best estimate)
   - #1 *
   - #2 *
4. Diagnosis for use (indication)
   - #1 Sinus headache
   - #2 sinus headache
5. Event abated after use stopped or dose reduced
   - #1 yes no doesn't apply
   - #2 yes no doesn't apply
6. Lot # (if known)
   - #1 *
   - #2 *
7. Exp. date (if known)
   - #1 *
   - #2 *
8. Event reappeared after reintroduction
   - #1 yes no doesn't apply
   - #2 yes no doesn't apply
9. NDC # - for product problems only (if known)
   - #1 NI
   - #2 NI
10. Concomitant medical products and therapy dates (exclude treatment of event)

G. All manufacturers

1. Contact office - name/address (& mfring site for devices)

Bayer Corporation
Pharmaceutical Division
400 Morgan Lane
West Haven, CT 06516-4175

2. Phone number: 888-765-3203
3. Report source (check all that apply)
   - foreign
   - study
   - literature
   - consumer
   - health professional
   - user facility
   - company representative
   - distributor
   - other: *
4. Date received by manufacturer (mo-day-yr): 01-OCT-2001
5. (A)NDA # 21-076
   - IND #
   - PLA #
   - pre-1938 yes
   - OTC product yes
6. If IND, protocol #
7. Type of report (check all that apply)
   - 5-day 15-day
   - 10-day periodic
   - Initial follow-up #
8. Adverse event term(s)

NERVOUSNESS, SWEATING, ABDOMINAL PAIN, GASTROINTESTINAL HEMORRHAGE, GASTROINTESTINAL HEMORRHAGE

9. Mfr. report number: 200111977BCC

E. Initial reporter

1. Name, address & phone #

Mr. [redacted]
[redacted] Road
[redacted] UNITED STATES
Phone: [redacted]

2. Health professional? yes no
3. Occupation: NI
4. Initial reporter also sent report to FDA: yes no unk

FDA

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

Item completed on continuation pages.

DEC 21 2001

B.5. Describe event or problem

[continuation:] 220/120 mg on 28-SEP-2001. He also reported taking Advil (ibuprofen) 400 mg right after taking the Aleve Sinus and Headache. The consumer experienced the events SHAKINESS and BEGAN TO SWEAT within four hours after taking the products. The consumer also experienced the event of STOMACH PAIN and said he had STOMACH BLEEDING which he thinks has been caused by the products. He discontinued use and his symptoms subsided on 29-SEP-2001. On 30-SEP-2001, at approximately 10:30 PM, he proceeded to take another Aleve Sinus and Headache followed by two more Advil. The consumer reported waking up on 01-OCT-2001 at about 1:30 A.M., feeling shaky and sweaty. The consumer stated he continues to experience these symptoms as of 01-OCT-2001. No further information was provided.

Bayer global comment:
The event STOMACH BLEEDING with the symptom of blood in stool is serious (medically important) and listed in the U.S. Product Information for Aleve Sinus and Headache (naproxen sodium / pseudoephedrine HCl). The event SHAKINESS is non-serious and is not listed. The events BEGAN TO SWEAT and STOMACH PAIN are non-serious and are listed. Based on the information provided for this case, a causal relationship between the events and naproxen sodium/pseudoephedrine HCl administration cannot be excluded. This view is supported by a positive temporal association and a positive rechallenge for the events SHAKINESS and BEGAN TO SWEAT. However, the consumer reports taking 400 mg of ibuprofen in addition to the Aleve Sinus and Headache. This may be a possible alternative explanation. More information will be requested.

C.2. Dose, frequency & route used (Suspect #1)

Drug name: Aleve Sinus & Headache Caplets

Dose, frequency and route	Therapy dates	Lot number	Exp. date
220/120 MG ONCE ORAL	28-SEP-2001	230231F	??-MAY-2003
220/120 MG ONCE ORAL	30-SEP-2001	230231F	??-MAY-2003

C.3. Therapy dates (if unknown, give duration) (mo/day/yr) (Suspect #1)

See table of dose information for C-2 above

C.6. Lot # (if known) (Suspect #1)

See table of dose information for C-2 above

C.7. Exp. date (if known) (mo/day/yr) (Suspect #1)

See table of dose information for C-2 above

3848262-3-00-03

oration

MED WATCH	A.1. Patient Identifier [redacted]	G.9. Mfr. report number 200111977BCC	Page 3 of 3

C.2. Dose, frequency & route used (Suspect #2)

Drug name: Advil (IBUPROFEN)

Dose, frequency and route	Therapy dates	Lot number	Exp. date
400 MG ONCE ORAL	28-SEP-2001	NI	NI
400 MG ONCE ORAL	30-SEP-2001	NI	NI

C.3. Therapy dates (if unknown, give duration) (mo/day/yr) (Suspect #2)

See table of dose information for C-2 above

C.6. Lot # (if known) (Suspect #2)

See table of dose information for C-2 above

C.7. Exp. date (if known, mo/day/yr) (Suspect #2)

See table of dose information for C-2 above

G.3. Report source (other)

BAYER CONSUMER CARE USA

DEC 21 2001

RECEIVED AT DRUG SAFETY SURVEILLANCE

16-JUL-1998-0957

MEDWATCH

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

Individual Safety Report

3187477-7-00-01

McNEIL CONSUMER PRODUCTS COMPANY
FORT WASHINGTON, PA 19034

Page ____ of ____

FDA use only

A Patient information

1. Patient identifier	2. Age at time of event:	3. Sex	4. Weight
[redacted] in confidence	34 mo or Date of birth: 05/15/95	( )female (X)male	unk lbs or kgs

B Adverse event or product problem

1. X Adverse event and/or Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)

( ) death (mo/day/yr)
( ) life-threatening
(X) hospitalization - initial or prolonged
( ) disability
( ) congenital anomaly
( ) required intervention to prevent permanent impairment/damage
(X) other: recovered

3. Date of event (mo/day/yr)	4. Date of this report (mo/day/yr)
4/98	05/12/98

5. Describe event or problem

Notification via company sales representative of physician report of MELENA & HEMATEMESIS allegedly associated w/the use of Children's Motrin® Ibuprofen Oral Suspension in a male patient. According to physician, mother gave patient Children's Motrin 100 mg every 4 hours primarily on empty stomach for a high fever. Two & one-half days later, patient taken to the emergency room w/blood in stool, bleeding from mouth, & vomiting. Patient sent to 2nd hospital, seen by pediatric gastroenterologist,admitted & endoscopy performed. Addl info rec'd 5/13/98:Pediatric gastroenterologist reports patient received a blood transfusion & was treated w/PEPCIDE IV for two days,then PRILOSEC®. Endoscopy showed ulcerations in stomach (STOMACH ULCER).Addl info rec'd 6/19/98:Discharge Form from hospital indicates patient rec'd multiple 100 mg doses of Motrin over 4 day period w/minimal food intake. Hematemesis x3 prior to admission. Patient admitted to hospital on 4/4/98. On 4/5/98, patient hemodynamically stable & discharged w/principle diagnosis of hematemesis & GASTRITIS.

6. Relevant tests/laboratory data, including dates

On 4/5/98: Hct=12.8, Hgb=36.3; EGD reportedly showed ulcerations in stomach, biopsy results not provided

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

unknown

C Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)

#1 Children's Motrin Ibuprofen Oral Suspen
#2

2. Dose, frequency & route used	3. Therapy dates (if unknown, give duration) from/to (or best estimate)
#1 100 mg, q4h, po	#1 2.5 days
#2	#2

4. Diagnosis for use (indication)

#1 high fever
#2

5. Event abated after use stopped or dose reduced

#1 (X) Yes ( ) No ( ) N/A
#2 ( ) Yes ( ) No ( ) N/A

6. Lot # (if known)	7. Exp. date (if known)
#1 Unknown	#1 Unknown
#2	#2

8. Event reappeared after reintroduction

#1 ( ) Yes ( ) No (X) N/A
#2 ( ) Yes ( ) No ( ) N/A

9. NDC # - for product problems only (if known)

- -

10. Concomitant medical products and therapy dates (exclude treatment of event)

unknown

G All manufacturers

1. Contact office - name/address (& mfring site for devices)

McNeil Consumer Products Company
Medical Affairs
7050 Camp Hill Road
Ft. Washington, PA 19034

2. Phone number: 215-233-7820

3. Report source (check all that apply)

( ) foreign
( ) study
( ) literature
( ) consumer
(X) health professional
( ) user facility
( ) company representative
( ) distributor
( ) other:

4. Date received by manufacturer (mo/day/yr): 05/08/98

5. (A) NDA # 20-516
IND #
PLA #
pre-1938 ( ) Yes
OTC product (X) Yes

6. If IND, protocol #

7. Type of report (check all that apply)

( ) 5-day ( )15-day
( ) 10-day (X)periodic
(X) initial ( )follow-up #

8. Adverse event term(s)

ULCER STOMACH
MELENA
HEMATEMESIS
GASTRITIS

9. Mfr. report number

0977561A

F Initial reporter

1. Name, address & phone #

[redacted]

2. Health professional?	3. Occupation	4. Initial reporter also sent report to FDA
(X) Yes ( ) No	gastroenterolog	( ) Yes ( ) No (X) Unk

FDA Form 3500A

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

JUL 17 1998

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Individual Safety Report

3221540-7-00-01

Generated by AEmanager™ from PCSI, Inc. For use by user-facilities, distributors and manufacturers for MANDATORY reporting

Form Approved: OMB No. 0910-0291 Expires:4/30/98
FDA Facsimile approval: 04/10/1998

Mfr. report # INT1990046

UF/Dist report #

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

Patient information

1. Patient identifier: [redacted] In confidence
2. Age at time of event: UNK or Date of birth:
3. Sex: ☑ female ☐ male
4. Weight: UNK lbs or kgs

B. Adverse event or product problem

1. ☑ Adverse event and/or ☐ Product Problem (e.g. defects/malfunctions)

2. Outcome attributed to adverse event (check all that apply)
☐ Death (mo/day/yr)
☐ Life-Threatening
☐ Hospitalization - initial or prolonged
☐ Disability
☐ Congenital Anomaly
☑ Required intervention to prevent permanent impairment/damage
☑ Other: MEDICALLY SIGNIFICANT

3. Date of event (mo/day/yr): 02/07/1999
4. Date of this report (mo/day/yr): 02/12/1999

5. Describe event or problem

A report of GI hemorrhage was received. A female patient was hospitalized and received front loaded tPA and was started on a heparin drip on 06-Feb-1999. She continued to have chest pain and was transferred t[redacted] On 07-Feb the chest pain was continuing and she received Integrilin. She was also receiving heparin at the time. At some time during the day she developed melena and was transfused with 2 units of blood. She was diagnosed with gastrointestinal bleeding considered to be related to NSAID consumption as she had been taking copious amounts of Advil for back pain prior to admission.

6. Relevant tests/laboratory data, including dates

7. Other relevant history, including preexisting medical conditions (e.g. allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)
DIABETES; SMOKING; HAD BEEN TAKING COPIOUS AMOUNTS OF ADVIL FOR BACK PAIN

C. Suspect medication(s)

FDA Use Only

1. Name (give labeled strength & mfr/labeler, if known)
#1 INTEGRILIN (EPTIFIBATIDE) INJECTION INJECTABLE SOLUTION
#2 ADVIL

2. Dose, frequency & route used
#1 INTRAVENOUS
#2

3. Therapy dates (if unknown, give duration) from/to (or best estimate)
#1 02/07/1999- --/--/----
#2

4. Diagnosis for Use (indication)
#1 CHEST PAIN
#2 BACK PAIN

5. Event abated after use stopped or dose reduced
#1 ☐ yes ☐ no ☑ doesn't apply
#2 ☐ yes ☐ no ☑ doesn't apply

6. Lot # (if known)
#1
#2

7. Exp. date (if known)
#1
#2

8. Event reappeared after reintroduction
#1 ☐ yes ☐ no ☑ doesn't apply
#2 ☐ yes ☐ no ☑ doesn't apply

9. NDC # - for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)
HEPARIN ; RT-PA

G. All manufacturers

1. Contact office-name / address (& mfr/labeler site for devices)
COR THERAPEUTICS, INC.
256 EAST GRAND AVENUE
SOUTH SAN FRANCISCO, CA 94080

2. Phone Number: 650-244-6800

3. Report Source (check all that apply)
☐ foreign
☐ study
☐ literature
☑ health professional
☐ user facility
☐ company representative
☐ distributor
☐ consumer
☐ other:

4. Date received by manufacturer (mo/day/yr): 02/12/1999

5. (A) NDA # 20-718
IND #
PLA #
pre-1938 ☐ yes
OTC product ☐ yes

6. If IND, protocol #

7. Type of report (check all that apply)
☐ 5-day ☐ 15-day
☐ [illegible]y ☑ periodic
☑ Initial ☐ follow-up#

8. Adverse Event Term(s)
MELAENA

9. Mfr. report number
INT1990046

MAR 12 1999

E. Initial reporter

1. Name, address, and phone #
[redacted] M.D. [redacted]
UNITED STATES

2. Health Professional?
☑ yes ☐ no

3. Occupation
MEDICAL DOCTOR

4. Initial reporter also sent report to FDA
☐ yes ☐ no ☑ unk

3500A Facsimile

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

MEDWATCH
Individual Safety Report
3225666-3-00-01

for VOLUNTARY reporting by health professionals of adverse events and product problems

CDER

Page ___ of ___

CDER

FDA Use Only — See OMB statement on reverse
Triage unit sequence # 99836

A. Patient information

1. Patient identifier: [redacted]8049 (confidence)
2. Age at time of event: 70 or Date of birth:
3. Sex: ☐ female ☒ male
4. Weight: ___ lbs or ___ kgs

B. Adverse event or product problem

1: ☒ Adverse event and/or ☐ Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)
☐ death ___ (mo/day/yr)
☐ life-threatening
☒ hospitalization - initial or prolonged
☐ disability
☐ congenital anomaly
☐ required intervention to prevent permanent impairment/damage
☐ other: ___

3. Date of event (mo/day/yr): 11/17/98
4. Date of this report (mo/day/yr): 11/20/98

5. Describe event or problem

Patient had black stools since Sunday 11/15/98 - came into the ER on 11/17/98 - hypotensive, black stool, ↓ HCT. Had EGD performed - found an ulcer on the bulb of the duodenum, duodenitis, gastritis. Patient had a (+) CLO test for H. pylori. Started on Iansoprazole and triple therapy for H. pylori

DSS

MAR 2 5 1999

ADVERSE EVENT REPORTING SYSTEM

6. Relevant tests/laboratory data, including dates

	HCT
11/17/98	40
11/17/98	32
11/20/98	37

baseline HCT > 6 months prior 47

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

Sleep Apnea

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
#1 Ibuprofen 200mg
#2 Aspirin 325mg

2. Dose, frequency & route used
#1 6-8 tablets QWK
#2 2-3 tablets QWK

3. Therapy dates (if unknown, give duration) from/to (or best estimate)
#1 ~several months
#2 ~several months

4. Diagnosis for use (indication)
#1 Aches/Pains
#2 Heart

5. Event abated after use stopped or dose reduced
#1 ☒ yes ☐ no ☐ doesn't apply
#2 ☒ yes ☐ no ☐ doesn't apply

6. Lot # (if known)
#1
#2

7. Exp. date (if known)
#1
#2

8. Event reappeared after reintroduction
#1 ☐ yes ☐ no ☒ doesn't apply
#2 ☐ yes ☐ no ☒ doesn't apply

9. NDC # (for product problems only)
- -

10. Concomitant medical products and therapy dates (exclude treatment of event)
None.

D. Suspect medical device

1. Brand name
2. Type of device
3. Manufacturer name & address
RECD.
MAR 23 1999
4. Operator of device
☐ health professional
☐ lay user/patient
☐ other: ___

6. model # MEDWATCH CTU
catalog #
serial #
lot #
other #

5. Expiration date (mo/day/yr)
7. If implanted, give date (mo/day/yr)
8. If explanted, give date (mo/day/yr)

9. Device available for evaluation? (Do not send to FDA)
☐ yes ☐ no ☐ returned to manufacturer on ___ (mo/day/yr)

10. Concomitant medical products and therapy dates (exclude treatment of event)

E. Reporter (see confidentiality section on back)

1. Name, address & phone #
CLINICAL PHARMACY
V.A. MEDICAL CENTER
500 FOURTH AVENUE
SALT LAKE CITY, UTAH 84148
(801) 582-1565 ext. 2172

2. Health professional? ☒ yes ☐ no
3. Occupation: RPh

4. Also reported to
☐ manufacturer
☐ user facility
☐ distributor

5. If you do NOT want your identity disclosed to the manufacturer, place an "X" in this box. ☐

FDA

Mail to: MEDWATCH, 5600 Fishers Lane, Rockville, MD 20852-9787
or FAX to: 1-800-FDA-0178

FDA Form 3500 (6/93)

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

99836